

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Daniel Davis Examiner #: 79061 Date: 8/15/04  
 Art Unit: 3731 Phone Number 30 5-1232 Serial Number: 09/872526  
 Mail Box and Bldg/Room Location: \_\_\_\_\_ Results-Format Preferred (circle) PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: \_\_\_\_\_

Inventors (please provide full names): \_\_\_\_\_

Earliest Priority Filing Date: \_\_\_\_\_

*\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

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Date Searcher Picked Up: _____	Bibliographic _____	Dr.Link _____
Date Completed: _____	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: _____	Fulltext _____	Sequence Systems _____
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FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004

=> file medline

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FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

FILE LAST UPDATED: 17 JUL 2004 (20040717/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD  
for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2004 vocabulary. See <http://www.nlm.nih.gov/mesh/> and  
[http://www.nlm.nih.gov/pubs/techbull/nd03/nd03\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html) for a  
description of changes.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

```
=> s fetal tissue
    215418 FETAL
      6 FETALS
    215420 FETAL
      (FETAL OR FETALS)
    771399 TISSUE
    241182 TISSUES
    916794 TISSUE
      (TISSUE OR TISSUES)
L1      6659 FETAL TISSUE
      (FETAL(W) TISSUE)
```

```
=> s in utero or donor
    15160 UTERO
      1 UTEROS
    15160 IN UTERO
      (UTERO OR UTEROS)
    75880 DONOR
    77222 DONORS
    131598 DONOR
      (DONOR OR DONORS)
L2      146532 IN UTERO OR DONOR
```

```
=> s percutan?
L3      59250 PERCUTAN?
```

```
=> s l1 (S) l2 (S) 3
    2640231 3
L4      2 L1 (S) L2 (S) 3
```

```
=> d 1-2 ibib abs
```

```
L4  ANSWER 1 OF 2      MEDLINE on STN
ACCESSION NUMBER:      2002728303      MEDLINE
DOCUMENT NUMBER:      PubMed ID: 12489998
TITLE:      A preliminary evaluation of recombinant adeno-associated
              virus biodistribution in rhesus monkeys after intrahepatic
              inoculation in utero.
AUTHOR:      Lai Lihui; Davison Billie B; Veazey Ronald S; Fisher
              Krishna J; Baskin Gary B
CORPORATE SOURCE:      Division of Comparative Pathology, Tulane National Primate
              Research Center, 18703 Three Rivers road, Covington, LA
              70433, USA.
CONTRACT NUMBER:      RR 00164 (NCRR)
SOURCE:      Human gene therapy, (2002 Nov 20) 13 (17) 2027-39.
              Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY:      United States
DOCUMENT TYPE:      (EVALUATION STUDIES)
              Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:      English
FILE SEGMENT:      Priority Journals
ENTRY MONTH:      200308
ENTRY DATE:      Entered STN: 20021220
              Last Updated on STN: 20030805
              Entered Medline: 20030804
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AB  The ability to deliver genes to fetuses in utero may prove crucial for
      those genetic diseases that are associated with severe fetal morbidity and
      for which there is no effective postnatal therapy. In utero therapy may
      be especially useful in diseases that affect the central nervous system
      because the immature blood-brain barrier may facilitate gene delivery to
      neural target cells. We investigated whether in utero inoculation of
      recombinant adeno-associated virus (rAAV) into rhesus monkey fetuses would
      be a useful method of gene delivery, especially to the central nervous
      system. When the monkeys were sacrificed after birth, we found vector
      genomes distributed in many tissues, including the brain and peripheral
      blood. Pericapillary astrocytes expressing transgene products were
      detected by immunohistochemistry. In addition, we occasionally found
      vector genomes in the maternal blood. No adverse clinical or pathologic
      effects were observed in the inoculated monkeys. We concluded that (1) in
      utero intrahepatic inoculation of rAAV is a potentially safe and
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useful method of delivering genes to many **fetal tissues**  
; (2) astrocytes may be the cell type most easily targeted in the central nervous system (CNS) after systemic administration; and (3) the potential of inadvertent gene transfer to the mother must be considered.

L4 ANSWER 2 OF 2 MEDLINE on STN  
ACCESSION NUMBER: 90066183 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2586398  
TITLE: Neural fetal tissue transplantation. Should we do what we can do?.  
AUTHOR: Mahowald M B  
CORPORATE SOURCE: Case Western Reserve University School of Medicine, Cleveland, Ohio.  
SOURCE: Neurologic clinics, (1989 Nov) 7 (4) 745-57.  
Journal code: 8219232. ISSN: 0733-8619.  
Report No.: KIE-35138.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Bioethics; Priority Journals  
ENTRY MONTH: 199001  
ENTRY DATE: Entered STN: 19900328  
Last Updated on STN: 20030318  
Entered Medline: 19900104

AB The following factors are relevant to ethical considerations regarding fetal tissue transplantation for treatment of neurological disorders: the empirical status of human fetuses or abortuses, different purposes and sites of tissue retrieval or implantation, the therapeutic potential of the technique, the means through which tissue becomes available, possible motives, and possible donors and recipients of transplant tissue. After examining each of these, the author concludes that (1) only dead fetuses should be used as tissue sources, (2) decisions regarding abortion and transplantation should be kept separate, (3) anonymity between **donor** and recipient should be observed, and (4) buying and selling of **fetal tissue** should not be permitted.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
L2 146532 S IN UTERO OR DONOR  
L3 59250 S PERCUTAN?  
L4 2 S L1 (S) L2 (S) 3

=> s l1 (S) l2 (S) l3  
L5 0 L1 (S) L2 (S) L3

=> s l1 (S) l2  
L6 60 L1 (S) L2

=> s incision  
19657 INCISION  
5641 INCISIONS  
L7 23472 INCISION  
(INCISION OR INCISIONS)

=> s l1 (S) l2 (S) l7  
L8 0 L1 (S) L2 (S) L7

=> s transplant?  
L9 354581 TRANSPLANT?

=> s l1 (S) l2 (S) l9  
L10 14 L1 (S) L2 (S) L9

=> d 1-14 ibib abs

L10 ANSWER 1 OF 14 MEDLINE on STN

ACCESSION NUMBER: 2004353039 IN-PROCESS  
DOCUMENT NUMBER: PubMed ID: 15256967  
TITLE: **Fetal tissue banking for transplantation: characteristics of the donor population and considerations for donor and tissue screening.**  
AUTHOR: Newman-Gage H; Bravo D; Holmberg L; Mason J; Eisenhower M; Nekhani N; Fantel A  
CORPORATE SOURCE: Northwest Tissue Center/Puget Sound Blood Center, Seattle, WA, USA; 921 Terry Avenue, Seattle, WA 98104, USA (Phone/Fax: (206) 292-2317 (206) 343-1776).  
SOURCE: Cell Tissue Bank, (2000) 1 (1) 45-53.  
Journal code: 100965121. ISSN: 1389-9333.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals  
ENTRY DATE: Entered STN: 20040717  
Last Updated on STN: 20040717

AB We initiated this study to evaluate the suitability for therapeutic use in transplantation of tissues obtained from human abortuses. We have developed protocols for the collection, handling and preservation of hepatic stem cells from electively aborted embryos and have developed methods for assessment of the cells so derived and processed. In this paper we present our findings regarding screening of potential donors, acquisition of fetal tissues, and assessment of the tissues for potentially infectious contaminants. We assess the suitability of the tissue donors according to current standards used for donors of commonly transplanted tissues (e.g., bone grafts, skin grafts and heart valves) and present data regarding the real availability of tissues from elective abortion procedures that would meet those standard tissue banking criteria. We specifically evaluated the donor's willingness to provide a blood sample for testing, conducted a detailed interview similar to those used for typical organ and tissue donors, and assessed the type and incidence of contamination in collected tissues. We find that although many women are willing to consent to use of the tissues for transplantation, attrition from the study for various reasons results in few fetal organs ultimately realistically available for transplantation. Typical reasons for attrition include: unwillingness to have a blood sample drawn or tested, positive serology results, social/medical high risk factors for acquisition of transmissible disease, no identifiable organs available, and unacceptable microbial contamination. Thus, although it might seem that due to the numbers of abortions performed annually, that there would be substantial numbers of suitable tissues available, only a small proportion are truly suitable for transplantation.

L10 ANSWER 2 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 1999439259 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10511241  
TITLE: Isolation and intracerebral grafting of nontransformed multipotential embryonic human CNS stem cells.  
AUTHOR: Vescovi A L; Gritti A; Galli R; Parati E A  
CORPORATE SOURCE: National Neurological Institute C. Besta, Milan, Italy.. vescovi@tin.it  
SOURCE: Journal of neurotrauma, (1999 Aug) 16 (8) 689-93.  
Journal code: 8811626. ISSN: 0897-7151.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199911  
ENTRY DATE: Entered STN: 20000111  
Last Updated on STN: 20000111  
Entered Medline: 19991124

AB In this work, we show that the embryonic human brain contains multipotent central nervous system (CNS) stem cells, which may provide a continuous, standardized source of human neurons that could virtually eliminate the use of primary human fetal brain tissue for intracerebral transplantation. Multipotential stem cells can be isolated from the developing human CNS in a reproducible fashion and can be exponentially expanded for longer than 2 years. This allows for the establishment of continuous, nontransformed

neural cell lines, which can be frozen and banked. By clonal analysis, reverse transcription polymerase chain reaction, and electrophysiological assay, we found that over such long-term culturing these cells retain both multipotentiality and an unchanged capacity for the generation of neuronal cells, and that they can be induced to differentiate into catecholaminergic neurons. Finally, when transplanted into the brain of adult rodents immunosuppressed by cyclosporin A, human CNS stem cells migrate away from the site of injection and differentiate into neurons and astrocytes. No tumor formation was ever observed. Aside from depending on scarce human neural **fetal tissue**, the use of human embryonic CNS stem cells for clinical neural **transplantation** should provide a reliable solution to some of the major problems that pertain to this field, and should allow determination of the safety characteristics of the **donor** cells in terms of tumorigenicity, viability, sterility, and antigenic compatibility far in advance of the scheduled day of surgery.

L10 ANSWER 3 OF 14 MEDLINE on STN  
 ACCESSION NUMBER: 1998231886 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 9572176  
 TITLE: Fetal tissue typing in anticipation of neonatal heart transplantation.  
 AUTHOR: Gilles J M; Burkett G; Perryman R A; Ferrer P L  
 CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Miami School of Medicine, Florida 33101-6960, USA.  
 SOURCE: Obstetrics and gynecology, (1998 May) 91 (5 Pt 2) 823-5. Journal code: 0401101. ISSN: 0029-7844.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: (CASE REPORTS)  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199805  
 ENTRY DATE: Entered STN: 19980520  
 Last Updated on STN: 19980520  
 Entered Medline: 19980514

AB BACKGROUND: Hypoplastic left heart syndrome is among the most common major congenital cardiac anomalies. Fetuses with this anomaly survive but require either reconstructive surgery or heart transplantation postnatally. CASE: A woman whose fetus was diagnosed with hypoplastic left heart syndrome underwent funipuncture for fetal tissue typing. The fetus then was listed for heart transplantation. Once an ABO-compatible donor heart was procured, the fetus was delivered and immediately underwent transplantation. CONCLUSION: In candidates for neonatal heart **transplantation**, **fetal tissue** typing allows the search for an ABO-compatible **donor** heart to begin earlier. This approach minimizes the morbidity associated with postnatal waiting and allows transplantation to take place while the neonate is less immunocompetent.

L10 ANSWER 4 OF 14 MEDLINE on STN  
 ACCESSION NUMBER: 97387601 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 9243621  
 TITLE: Medial fetal ventral mesencephalon: a preferred source for dopamine neuron grafts.  
 AUTHOR: Costantini L C; Lin L; Isacson O  
 CORPORATE SOURCE: Neuroregeneration Laboratory, Harvard Medical School, McLean Hospital, Belmont, MA 02178, USA.  
 SOURCE: Neuroreport, (1997 Jul 7) 8 (9-10) 2253-7. Journal code: 9100935. ISSN: 0959-4965.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199710  
 ENTRY DATE: Entered STN: 19971021  
 Last Updated on STN: 19990129  
 Entered Medline: 19971007

AB Currently, **fetal tissue transplantation** into patients with Parkinson's disease utilizes the entire ventral mesencephalon (VM) as **donor** tissue. However, the resulting mixture of cell types contains a relatively low proportion of

therapeutically relevant dopamine (DA) neurons. We show that differential dissection of a medial region of embryonic day 14 rat VM yields a significantly higher proportion of DA neurons (8-10%) than is found in lateral VM (2%) or whole VM (4-5%). Medial VM also contained a larger number of the specific subpopulation of DA neurons (aldehyde dehydrogenase-positive; AHD) that project to dorsolateral motor region of the striatum. Selective dissection of fetal medial VM selectively enriches DA neurons in cell preparations useful for transplantation in Parkinson's disease.

L10 ANSWER 5 OF 14 MEDLINE on STN  
 ACCESSION NUMBER: 97208925 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 9055867  
 TITLE: Histological evidence of fetal pig neural cell survival after transplantation into a patient with Parkinson's disease.  
 AUTHOR: Deacon T; Schumacher J; Dinsmore J; Thomas C; Palmer P; Kott S; Edge A; Penney D; Kassissieh S; Dempsey P; Isacson O  
 CORPORATE SOURCE: Neuroregeneration Laboratory, Harvard Medical School, McLean Hospital MRC 119, Belmont, Massachusetts 02178, USA.  
 SOURCE: Nature medicine, (1997 Mar) 3 (3) 350-3.  
 Journal code: 9502015. ISSN: 1078-8956.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: (CASE REPORTS)  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199704  
 ENTRY DATE: Entered STN: 19970414  
 Last Updated on STN: 19970414  
 Entered Medline: 19970401

AB The movement disorder in Parkinson's disease results from the selective degeneration of a small group of dopaminergic neurons in the substantia nigra pars compacta region of the brain. A number of exploratory studies using human fetal tissue allografts have suggested that transplantation of dopaminergic neurons may become an effective treatment for patients with Parkinson's disease and the difficulty in obtaining human fetal tissue has generated interest in finding corresponding non-human donor cells. Here we report a post-mortem histological analysis of fetal pig neural cells that were placed unilaterally into the caudate-putamen brain region of a patient suffering from Parkinson's disease. Long-term (over seven months) graft survival was found and the presence of pig dopaminergic neurons and other pig neural and glial cells is documented. Pig neurons extended axons from the graft sites into the host brain. Furthermore, other graft derived cells were observed several millimeters from the implantation sites. Markers for human microglia and T-cells showed only low reactivity in direct proximity to the grafts. This is the first documentation of neural xenograft survival in the human brain and of appropriate growth of non-human dopaminergic neurons for a potential therapeutic response in Parkinson's disease.

L10 ANSWER 6 OF 14 MEDLINE on STN  
 ACCESSION NUMBER: 96393740 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 8800513  
 TITLE: A mathematical model for the estimation of human embryonic and fetal age.  
 AUTHOR: Evtouchenko L; Studer L; Spenger C; Dreher E; Seiler R W  
 CORPORATE SOURCE: Department of Neurosurgery, University of Bern, Inselspital, Switzerland.  
 SOURCE: Cell transplantation, (1996 Jul-Aug) 5 (4) 453-64.  
 Journal code: 9208854. ISSN: 0963-6897.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199702  
 ENTRY DATE: Entered STN: 19970305  
 Last Updated on STN: 19970305  
 Entered Medline: 19970220

AB Precise determination of donor age in human embryonic and fetal tissue is crucial for cell transplantation due to the existence of distinct time windows within which successful grafting is possible. This study demonstrates that between 4-12 wk postconception embryonic and fetal age can be estimated based on various morphometric parameters measured on a routine basis in suction abortion material. The greatest length, the neck-rump length, the foot length, and the proximal and distal arm and leg length were correlated with the anamnestic and ultrasonographically estimated age. Multivariate regression analyses showed a linear correlation between age and the logarithmic value of the various morphometric parameters. The best correlation was found for a mathematical model combining the limb parameters ( $r = 0.904$ ;  $p < 0.001$ ;  $n = 37$ ). A prospective follow-up study ( $n = 40$ ) was carried out to test the validity of the mathematical model. A high correlation was found between the calculated age and the estimated age based on anamnestic data ( $r = 0.749$ ,  $p < 0.001$ ). Outliers due to errors in the anamnestic data were readily identified by comparing anamnestic with calculated age. This method allows determination of embryonic and fetal age within and beyond the age group of the Carnegie classification and may, therefore, be useful for the needs of experimental and clinical cell transplantation.

L10 ANSWER 7 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 96304843 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8723798  
TITLE: Quo vadis? Fetal tissue transplantation.  
AUTHOR: Mischejda M  
CORPORATE SOURCE: Georgetown University Medical Center, Washington, DC 20007, USA.  
SOURCE: Journal of hematotherapy, (1996 Apr) 5 (2) 185-8. Ref: 31  
Journal code: 9306048. ISSN: 1061-6128.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199610  
ENTRY DATE: Entered STN: 19961022  
Last Updated on STN: 19990129  
Entered Medline: 19961009

AB The epidemiology and biologic characteristics of fetal tissue harvested from elective and spontaneous abortions are reviewed. The use of fetal bone marrow obtained from second trimester lost pregnancies is discussed. Allogeneic fetal tissue transplantation carried out in utero is reviewed. Data on intrauterine transplantation of human fetal bone marrow obtained from second trimester lost pregnancies into baboon fetuses are presented. The viability of this tissue, its clonogenic efficiency, engraftment, use in the future, and banking are discussed.

L10 ANSWER 8 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 95352172 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 7626187  
TITLE: Some contemporary ethical considerations related to organ transplantation.  
AUTHOR: Cohen B; D'Amato J  
CORPORATE SOURCE: Eurotransplant Foundation, Leiden, The Netherlands.  
SOURCE: Transplant international : official journal of the European Society for Organ Transplantation, (1995) 8 (3) 238-43.  
Ref: 22  
Journal code: 8908516. ISSN: 0934-0874.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199509  
ENTRY DATE: Entered STN: 19950921  
Last Updated on STN: 19950921



Entered Medline: 19950907

AB With the increasing number of transplantable organs and tissues, as well as improvements in transplantation results, has come a severe shortage of organ donors. Consequently, new ethical dilemmas, related to the fair allocation of available organs and the use of alternative sources of donor organs, are of growing concern. Establishing fair allocation priorities is a serious problem in organ transplantation. Ethically, they should be defined by society as a whole rather than exclusively by the medical profession. Proposed solutions for the organ donor shortage, each with their unique ethical constraints, include the use of related donors, partial organ transplantation, cell transplantation using fetal tissue, and the use of animal organs "xenotransplantation". Commercial trading in donor organs must be regarded as an unethical activity rather than an ethical dilemma since the donors are motivated by monetary rather than by humanitarian reasons. These ethical dilemmas could be largely avoided by an effective reduction in the severe shortage of postmortal organ donations.

L10 ANSWER 9 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 95090873 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 7998247  
TITLE: Human fetal tissue from spontaneous abortions as potential sources of donor tissue for cell transplantation therapy.  
AUTHOR: Low W C; Eastlund T; Verfaillie C; Hirschel M; Virnig B; Weese K; Norris B; Chrysler G; Peterson A; Forbes J  
CORPORATE SOURCE: University of Minnesota Medical School, Minneapolis.  
CONTRACT NUMBER: R24-HD-30511 (NICHD)  
SOURCE: Transplantation proceedings, (1994 Dec) 26 (6) 3500.  
Journal code: 0243532. ISSN: 0041-1345.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199501  
ENTRY DATE: Entered STN: 19950126  
Last Updated on STN: 19990129  
Entered Medline: 19950118

L10 ANSWER 10 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 92370131 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 1504675  
TITLE: Human embryo as a source of cells.  
AUTHOR: Edwards R G  
CORPORATE SOURCE: Churchill College, Cambridge, UK.  
SOURCE: Bone marrow transplantation, (1992) 9 Suppl 1 90-2. Ref: 0  
Journal code: 8702459. ISSN: 0268-3369.  
Report No.: PIP-079084; POP-00290827.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; Population  
ENTRY MONTH: 199209  
ENTRY DATE: Entered STN: 19921009  
Last Updated on STN: 20021101  
Entered Medline: 19920918

AB This paper discusses ethical issues concerning the use of fetal tissue in transplantation or for other purposes after spontaneous or elective abortion. The major problems of using fetal tissues in transplantation and research are often ethical. Despite this, the methods have been used in many countries for Digeorge's syndrome, hemopoietic disorders, brain grafting, making vaccines and many research purposes. Local and national ethical committees are now widespread, and legislation has been passed in some countries. Practitioners should be constantly aware of public concern that can arise over matters affecting conception and fetal life. Fetal tissue transplantation also raises many issues for donors, mothers and recipients, quite apart from the practitioners. Clinical teams doing abortion and investigators using

fetal tissue must be totally distinct. Requests for tissues must pass through the Tissue Bank, and its establishment has helped some deontologists (absolutist) to come to terms with the need for fetal tissue transplantation. The ethics of abortion and not fetal tissue research is often stated as the fundamental ethical problem to be solved when using fetal tissues for transplantation. In conclusion, the study suggests that legislation should regulate this field of research, that local ethical committees are essential as a source of advice, and that investigators must strive for the highest moral position and communicate their work widely and fully counsel their patients.

L10 ANSWER 11 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 90383751 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 1698219  
TITLE: Comparison of growth, neovascularization, and enzymatic function of fetal intestinal grafts in the omentum and renal capsule.  
AUTHOR: Tisinai K; Shedd F; Harris R; Unthank J; Grosfeld J; Abu-Dalu K; Grosfeld J  
CORPORATE SOURCE: Section of Pediatric Surgery, Indiana University Medical Center, Indianapolis.  
SOURCE: Journal of pediatric surgery, (1990 Aug) 25 (8) 914-6.  
Journal code: 0052631. ISSN: 0022-3468.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199010  
ENTRY DATE: Entered STN: 19901122  
Last Updated on STN: 19960129  
Entered Medline: 19901019

AB **Fetal tissues** are less immunogenic and may be a useful donor source for organ transplantation. This report compares the fate of fetal small bowel segments transplanted in the omentum and renal capsule of recipient syngeneic rats. Two-centimeter segments of fetal jejunum and ileum were obtained from 26 donor 19-day gestational age rat fetuses and transplanted into the subrenal capsule (n = 35) and omentum (n = 40) in syngeneic Fisher rats (weight, 150 g) as free grafts. No immunosuppression was used. At 2 weeks posttransplantation, the recipient rats underwent laparotomy and the grafts were evaluated for viability, growth, enzymatic function, and revascularization. Viable grafts were identified in 27 of 35 renal capsule grafts and 34 of 40 omental grafts. The order of magnitude of fetal growth in the omentum for jejunum was 16 +/- 10 versus ileum 23 +/- 9 (NS). However, in the renal capsule, ileal growth (15 +/- 6) was significantly greater than jejunum (8 +/- 5; P less than .01). Growth for both jejunal and ileal segments was greater in the omentum (P less than .02). The lumen of all omental grafts remained patent; however, 26 of 27 renal grafts had cystic dilatations and areas of obstruction. Microfil casts of the specimens showed vascular connections (neovascularization) between the graft and omentum, a normal serosal vascular pattern, and many submucosal capillary-like vessels. Maltase activity was measured in fetal grafts and compared with control pups bred on the same date as the donor animals. The grafts had a higher maltase level 33.4 +/- 34.6 mumol/min/g than controls 8.3 +/- 2.0 (P less than .005). (ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 12 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 90066183 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2586398  
TITLE: Neural fetal tissue transplantation. Should we do what we can do?.  
AUTHOR: Mahowald M B  
CORPORATE SOURCE: Case Western Reserve University School of Medicine, Cleveland, Ohio.  
SOURCE: Neurologic clinics, (1989 Nov) 7 (4) 745-57.  
Journal code: 8219232. ISSN: 0733-8619.  
Report No.: KIE-35138.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English

FILE SEGMENT: Bioethics; Priority Journals  
ENTRY MONTH: 199001  
ENTRY DATE: Entered STN: 19900328  
Last Updated on STN: 20030318  
Entered Medline: 19900104

AB The following factors are relevant to ethical considerations regarding **fetal tissue transplantation** for treatment of neurological disorders: the empirical status of human fetuses or abortuses, different purposes and sites of tissue retrieval or implantation, the therapeutic potential of the technique, the means through which tissue becomes available, possible motives, and possible donors and recipients of **transplant** tissue. After examining each of these, the author concludes that (1) only dead fetuses should be used as tissue sources, (2) decisions regarding abortion and **transplantation** should be kept separate, (3) anonymity between donor and recipient should be observed, and (4) buying and selling of **fetal tissue** should not be permitted.

L10 ANSWER 13 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 80219427 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 398203  
TITLE: [Restoration of mixed and severe immunologic deficiency, by fetal liver and thymus graft].  
Reconstitution d'un deficit immunitaire mixte et grave, par greffe de foie et de thymus foetaux.  
AUTHOR: Betend B; Touraine J L; Hermier M; Francois R  
SOURCE: Archives francaises de pediatrie, (1979 Dec) 36 (10) 995-1005.  
Journal code: 0372421. ISSN: 0003-9764.  
PUB. COUNTRY: France  
DOCUMENT TYPE: (CASE REPORTS)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: French  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198008  
ENTRY DATE: Entered STN: 19900315  
Last Updated on STN: 19900315  
Entered Medline: 19800825

AB A male infant with severe combined immunodeficiency but normal adenosine deaminase activity for whom no suitable bone marrow donor was available was given two separate grafts of both hepatic and thymic cells, the cells for each graft being taken from the same fetus aged 13 and 10 weeks respectively. Cell mediated and partial humoral immunity was restored 330 and 400 days respectively after the second transplant. No graft-versus-host reaction was observed and both red blood cell and lymphoid chimaerism could be demonstrated. The child was kept in strict bacterial isolation from the 3rd to the 537th day of life. Thirty months after the graft, the infant is in good health but has a defect of neutrophil chemotaxis and phagocytosis which requires prophylactic benzathine penicillin in addition to gammaglobulins. **Fetal tissue transplantation** may provide an alternative treatment for patients with severe combined immunodeficiency who do not have a histocompatible donor.

L10 ANSWER 14 OF 14 MEDLINE on STN  
ACCESSION NUMBER: 77230682 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 18618  
TITLE: Severe combined immunodeficiency disease. Characterization of the disease and results of transplantation.  
AUTHOR: Bortin M M; Rimm A A  
SOURCE: JAMA : journal of the American Medical Association, (1977 Aug 15) 238 (7) 591-600.  
Journal code: 7501160. ISSN: 0098-7484.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 197709  
ENTRY DATE: Entered STN: 19900314  
Last Updated on STN: 19950206  
Entered Medline: 19770922

AB Pretransplant and posttransplant data for 69 patients with severe combined immunodeficiency disease are presented. Both B and T lymphocyte functions were absent in approximately 80% of the children and markedly depressed in the remainder. **Transplantation** of marrow from HLA genotypically identical **donors** provided the highest six-month survival rate (63%); six-month survival rates for patients who received **fetal tissue transplants** (43%) or marrow from mixed leukocyte culture (MLC) negative **donors** (38%) were significantly higher (P less than .05) than for patients treated with marrow from MLC positive **donors** (5%). Additional factors appeared to influence survival and the severity of graft-vs-host (GVH) disease. Patients more than 6 months of age had more intense GVH disease than younger patients. Survival rates were lower and GVH disease more intense when boys received transplants from girl donors than the reverse.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
L2 146532 S IN UTERO OR DONOR  
L3 59250 S PERCUTAN?  
L4 2 S L1 (S) L2 (S) 3  
L5 0 S L1 (S) L2 (S) L3  
L6 60 S L1 (S) L2  
L7 23472 S INCISION  
L8 0 S L1 (S) L2 (S) L7  
L9 354581 S TRANSPLANT?  
L10 14 S L1 (S) L2 (S) L9

=> s suction or vacuum or suc?

13720 SUCTION  
37 SUCTIONS  
13733 SUCTION  
(SUCTION OR SUCTIONS)  
9680 VACUUM  
39 VACUUMS  
10 VACUA  
9702 VACUUM  
(VACUUM OR VACUUMS OR VACUA)  
1189525 SUC?  
L11 1197155 SUCTION OR VACUUM OR SUC?

=> s l1 (S) l2 (S) l9 (S) l11

L12 1 L1 (S) L2 (S) L9 (S) L11

=> d ibib abs

L12 ANSWER 1 OF 1 MEDLINE on STN  
ACCESSION NUMBER: 96393740 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8800513  
TITLE: A mathematical model for the estimation of human embryonic and fetal age.  
AUTHOR: Evtouchenko L; Studer L; Spenger C; Dreher E; Seiler R W  
CORPORATE SOURCE: Department of Neurosurgery, University of Bern, Inselspital, Switzerland.  
SOURCE: Cell transplantation, (1996 Jul-Aug) 5 (4) 453-64.  
Journal code: 9208854. ISSN: 0963-6897.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199702  
ENTRY DATE: Entered STN: 19970305  
Last Updated on STN: 19970305  
Entered Medline: 19970220

AB Precise determination of **donor** age in human embryonic and **fetal tissue** is crucial for cell **transplantation** due to the existence of distinct time windows within which

successful grafting is possible. This study demonstrates that between 4-12 wk postconception embryonic and fetal age can be estimated based on various morphometric parameters measured on a routine basis in suction abortion material. The greatest length, the neck-rump length, the foot length, and the proximal and distal arm and leg length were correlated with the anamnestic and ultrasonographically estimated age. Multivariate regression analyses showed a linear correlation between age and the logarithmic value of the various morphometric parameters. The best correlation was found for a mathematical model combining the limb parameters ( $r = 0.904$ ;  $p < 0.001$ ;  $n = 37$ ). A prospective follow-up study ( $n = 40$ ) was carried out to test the validity of the mathematical model. A high correlation was found between the calculated age and the estimated age based on anamnestic data ( $r = 0.749$ ,  $p < 0.001$ ). Outliers due to errors in the anamnestic data were readily identified by comparing anamnestic with calculated age. This method allows determination of embryonic and fetal age within and beyond the age group of the Carnegie classification and may, therefore, be useful for the needs of experimental and clinical cell transplantation.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

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L1      6659 S FETAL TISSUE
L2      146532 S IN UTERO OR DONOR
L3      59250 S PERCUTAN?
L4      2 S L1 (S) L2 (S) 3
L5      0 S L1 (S) L2 (S) L3
L6      60 S L1 (S) L2
L7      23472 S INCISION
L8      0 S L1 (S) L2 (S) L7
L9      354581 S TRANSPLANT?
L10     14 S L1 (S) L2 (S) L9
L11     1197155 S SUCTION OR VACUUM OR SUC?
L12     1 S L1 (S) L2 (S) L9 (S) L11
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=> s suction or vacuum or suc? or remov?

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13720 SUCTION
37 SUCTIONS
13733 SUCTION
(SUCTION OR SUCTIONS)
9680 VACUUM
39 VACUUMS
10 VACUA
9702 VACUUM
(VACUUM OR VACUUMS OR VACUA)
1189525 SUC?
255745 REMOV?
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L13 1406689 SUCTION OR VACUUM OR SUC? OR REMOV?

=> s 11 (S) 12 (S) 19 (S) 113

L14 1 L1 (S) L2 (S) L9 (S) L13

=> d ibib abs

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L14 ANSWER 1 OF 1      MEDLINE on STN
ACCESSION NUMBER: 96393740 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8800513
TITLE: A mathematical model for the estimation of human embryonic
and fetal age.
AUTHOR: Evtouchenko L; Studer L; Spenger C; Dreher E; Seiler R W
CORPORATE SOURCE: Department of Neurosurgery, University of Bern,
Inselspital, Switzerland.
SOURCE: Cell transplantation, (1996 Jul-Aug) 5 (4) 453-64.
Journal code: 9208854. ISSN: 0963-6897.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
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ENTRY MONTH: 199702  
ENTRY DATE: Entered STN: 19970305  
Last Updated on STN: 19970305  
Entered Medline: 19970220

AB Precise determination of **donor** age in human embryonic and **fetal tissue** is crucial for cell **transplantation** due to the existence of distinct time windows within which **successful** grafting is possible. This study demonstrates that between 4-12 wk postconception embryonic and fetal age can be estimated based on various morphometric parameters measured on a routine basis in suction abortion material. The greatest length, the neck-rump length, the foot length, and the proximal and distal arm and leg length were correlated with the anamnestic and ultrasonographically estimated age. Multivariate regression analyses showed a linear correlation between age and the logarithmic value of the various morphometric parameters. The best correlation was found for a mathematical model combining the limb parameters ( $r = 0.904$ ;  $p < 0.001$ ;  $n = 37$ ). A prospective follow-up study ( $n = 40$ ) was carried out to test the validity of the mathematical model. A high correlation was found between the calculated age and the estimated age based on anamnestic data ( $r = 0.749$ ,  $p < 0.001$ ). Outliers due to errors in the anamnestic data were readily identified by comparing anamnestic with calculated age. This method allows determination of embryonic and fetal age within and beyond the age group of the Carnegie classification and may, therefore, be useful for the needs of experimental and clinical cell transplantation.

=> s ?cutan?  
L15 247721 ?CUTAN?

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
L2 146532 S IN UTERO OR DONOR  
L3 59250 S PERCUTAN?  
L4 2 S L1 (S) L2 (S) 3  
L5 0 S L1 (S) L2 (S) L3  
L6 60 S L1 (S) L2  
L7 23472 S INCISION  
L8 0 S L1 (S) L2 (S) L7  
L9 354581 S TRANSPLANT?  
L10 14 S L1 (S) L2 (S) L9  
L11 1197155 S SUCTION OR VACUUM OR SUC?  
L12 1 S L1 (S) L2 (S) L9 (S) L11  
L13 1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?  
L14 1 S L1 (S) L2 (S) L9 (S) L13  
L15 247721 S ?CUTAN?

=> s 11 (S) 12 (S) 19 (S) 115  
L16 0 L1 (S) L2 (S) L9 (S) L15

=> s 11 (1) 12 (1) 19 (1) 115  
L17 0 L1 (L) L2 (L) L9 (L) L15

=> s 11 (1) 12 (1) 19 (1) 113  
L18 21 L1 (L) L2 (L) L9 (L) L13

=> d 1-21 ibib abs

L18 ANSWER 1 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 2004262523 IN-PROCESS  
DOCUMENT NUMBER: PubMed ID: 15161332  
TITLE: Is there a future for neural transplantation?.  
AUTHOR: Harrower Timothy P; Barker Roger A  
CORPORATE SOURCE: Cambridge Centre for Brain Repair, Forvie Site, Cambridge, UK.. DRSHarrower@aol.com  
SOURCE: BioDrugs : clinical immunotherapeutics, biopharmaceuticals and gene therapy, (2004) 18 (3) 141-53.

Journal code: 9705305. ISSN: 1173-8804.  
PUB. COUNTRY: New Zealand  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals  
ENTRY DATE: Entered STN: 20040527  
Last Updated on STN: 20040629

AB Traditionally neural **transplantation** has had as its central tenet the replacement of missing neurons that have been lost because of neurodegenerative processes, as exemplified by diseases such as Parkinson disease (PD). However, the effectiveness and widespread application of this approach clinically has been limited, primarily because of the poor donor supply of human fetal neural tissue and the incomplete neurobiological understanding of the circuit reconstruction required to normalize function in these diseases. So, in PD the progress from promising neural **transplantation** in animal models to proof-of-principle, open-labeled clinical **transplants**, to randomized, placebo-controlled studies of neural **transplantation** has not been straightforward. The emergence of previously undescribed adverse effects and lack of significant functional advantage in recent clinical studies has been disappointing and has served to cast a new, and perhaps more realistic, perspective on this treatment approach. In fact, there have been calls by some involved in neural **transplantation** to return to the drawing board before pressing on with further clinical trials, and the return to basic experimentation. This therefore precipitates the question - is there a future for neural **transplantation**? It is important to remember that there are a number of possible explanations for the disappointing results from the recent clinical trials in PD, ranging from the mode of **transplantation** to patient selection. Nevertheless, almost irrespective of these reasons for the current trial results, there have always been significant practical and ethical problems with using human **fetal tissue**, and so a number of alternative cell sources have been investigated. These alternative sources include stem cells, which are attractive for cell-based therapies because of their potential ease of isolation, propagation and manipulation, and their ability in some cases to migrate to areas of pathology and differentiate into specific and appropriate cell types. Furthermore, the availability of stem cells derived from non-embryonic sources (e.g. adult stem cells derived from the sub-ventricular zone) has **removed** some of the ethical limitations associated with the use of embryonic human tissue. These potentially beneficial aspects of stem cells means that there is a future for neural **transplantation** as a means of treating patients with a range of neurological disorders, although whether this will ever translate into a truly effective, widely available therapy remains unknown.

L18 ANSWER 2 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 2003573184 IN-PROCESS  
DOCUMENT NUMBER: PubMed ID: 14653615  
TITLE: Staging and preparation of human fetal striatal tissue for neural transplantation in Huntington's disease.  
AUTHOR: Rosser A E; Barker R A; Armstrong R J E; Elneil S; Jain M; Hurelbrink C B; Prentice A; Carne C; Thornton S; Hutchinson H; Dunnett S B  
CORPORATE SOURCE: School of Biosciences, Cardiff University, PO Box 911, Museum Av, Cardiff CF10 3US, Wales, UK.. RosserAE@cf.ac.uk  
SOURCE: Cell transplantation, (2003) 12 (7) 679-86.  
Journal code: 9208854. ISSN: 0963-6897.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals  
ENTRY DATE: Entered STN: 20031216  
Last Updated on STN: 20031216

AB **Transplantation** of human fetal central nervous system tissue has been shown to be of benefit in Parkinson's disease, and is currently being explored as a therapeutic option in Huntington's disease. The **success** of a neural **transplant** is dependent on a number of factors, including the requirement that **donor** cells are harvested within a given developmental window and that the cell

preparation protocols take account of the biological parameters identified in animal models. Although many of the criteria necessary for a **successful neural transplant** have been defined in animal models, ultimately they must be validated in human studies, and some issues can only ever be addressed in human studies. Furthermore, because **neural transplantation of human fetal tissue** is limited to small numbers of patients in any one surgical center, largely due to practical constraints, it is crucial that tissue preparation protocols are clearly defined and reproducible, so that (i) multicenter trials are possible and are based on consistent tissue preparation parameters, and (ii) results between centers can be meaningfully analyzed. Here we describe the preparation of human fetal striatum for **neural transplantation** in Huntington's disease, and report on the validation of a method for estimating the developmental stage of the fetus based on direct morphometric measurements of the embryonic tissue.

L18 ANSWER 3 OF 21 MEDLINE on STN  
 ACCESSION NUMBER: 2003479695 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 14557753  
 TITLE: Engraftment and tumor formation after allogeneic in utero transplantation of primate embryonic stem cells.  
 COMMENT: Comment in: Transplantation. 2003 Oct 15;76(7):1011-2. PubMed ID: 14584499  
 AUTHOR: Asano Takayuki; Ageyama Naohide; Takeuchi Koichi; Momoeda Mikio; Kitano Yoshihiro; Sasaki Kyoko; Ueda Yasuji; Suzuki Yutaka; Kondo Yasushi; Torii Ryuzo; Hasegawa Mamoru; Ookawara Shigeo; Harii Kiyonori; Terao Keiji; Ozawa Keiya; Hanazono Yutaka  
 CORPORATE SOURCE: Division of Genetic Therapeutics, Jichi Medical School, Tochigi, Japan.  
 SOURCE: Transplantation, (2003 Oct 15) 76 (7) 1061-7. Journal code: 0132144. ISSN: 0041-1337.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200312  
 ENTRY DATE: Entered STN: 20031015  
 Last Updated on STN: 20031219  
 Entered Medline: 20031202

AB BACKGROUND: To achieve human embryonic stem (ES) cell-based **transplantation** therapies, allogeneic **transplantation** models of nonhuman primates would be useful. We have prepared cynomolgus ES cells genetically marked with the green fluorescent protein (GFP). The cells were **transplanted** into the allogeneic fetus, taking advantage of the fact that the fetus is so immunologically immature as not to induce immune responses to **transplanted** cells and that **fetal tissue** compartments are rapidly expanding and thus providing space for the engraftment. METHODS: Cynomolgus ES cells were genetically modified to express the GFP gene using a simian immunodeficiency viral vector or electroporation. These cells were **transplanted in utero** with ultrasound guidance into the cynomolgus fetus in the abdominal cavity (n=2) or liver (n=2) at the end of the first trimester. Three fetuses were delivered 1 month after **transplantation**, and the other, 3 months after **transplantation**. Fetal tissues were examined for **transplanted** cell progeny by quantitative polymerase chain reaction and in situ polymerase chain reaction of the GFP sequence. RESULTS: A fluorescent tumor, obviously derived from **transplanted** ES cells, was found in the thoracic cavity at 3 months after **transplantation** in one fetus. However, **transplanted** cell progeny were also detected (approximately 1%) without teratomas in multiple **fetal tissues**. The cells were solitary and indistinguishable from surrounding host cells. CONCLUSIONS: **Transplanted** cynomolgus ES cells can be engrafted in allogeneic fetuses. The cells will, however, form a tumor if they "leak" into an improper space **such** as the thoracic cavity.

L18 ANSWER 4 OF 21 MEDLINE on STN  
 ACCESSION NUMBER: 2002599222 MEDLINE



DOCUMENT NUMBER: PubMed ID: 12344424  
TITLE: Chapter 173, Sections 1-2 of the 1989 Session Laws, 29 March 1989.  
AUTHOR: Anonymous  
CORPORATE SOURCE: United States. North Dakota.  
SOURCE: Annual review of population law, (1989) 16 44, 323-4.  
Journal code: 8008840. ISSN: 0364-3417.  
Report No.: ARPL-000475; PIP-078475; POP-00248510.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (LEGISLATION)  
LANGUAGE: English  
FILE SEGMENT: Population  
ENTRY MONTH: 199603  
ENTRY DATE: Entered STN: 20021101  
Last Updated on STN: 20021101  
Entered Medline: 19960307

AB In March of 1989, North Dakota passed legislation covering experimentation using live or dead fetuses. The law prohibits the use of any live human fetus, before or after birth, for any kind of experimentation. A human fetus can be studied while in **utero** if **such** procedures do not substantially jeopardize the life or health of the fetus and provided that there are no plans to abort said fetus. No fetus or newborn child or **fetal tissue** or organ may be used for research or **transplantation**. However, diagnostic or remedial procedures designed to determine or preserve the life or health of the fetus or the mother are allowed. No experiments can be conducted on a dead fetus resulting from an occurrence other than an induced abortion without the written consent of the mother who must be at least 18 years old. No fetus or **fetal tissue** resulting from an induced abortion can be used in **transplantation** except for diagnostic or remedial procedures for said fetus or its mother. No abortion can be performed if all or part of the consideration for the abortion is that fetal organs or tissue are to be used for **transplantation** or experimentation. No fetus or fetal organs (including embryos and neonates) can be sold or given away for a use in violation of this law.

L18 ANSWER 5 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 2001615282 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11645701  
TITLE: Ethics, public policy, and human fetal tissue transplantation research.  
AUTHOR: Childress James F  
SOURCE: Kennedy Institute of Ethics journal, (1991 Jun) 1 (2) 93-121.  
Journal code: 9109135. ISSN: 1054-6863.  
Report No.: KIE-33408.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Bioethics  
ENTRY MONTH: 199109  
ENTRY DATE: Entered STN: 20011105  
Last Updated on STN: 20021211  
Entered Medline: 19910917

AB This article focuses on the deliberations of the National Institutes of Health Human **Fetal Tissue Transplantation** Research Panel in 1988. It explores various arguments for and against the use of **fetal tissue** for **transplantation** research, following elective abortion, and for and against the use of federal funds for **such** research. After examining the relevance of various positions on the moral status of the fetus and the morality of abortion, the article critically examines charges that **such** research, especially with federal funds, would involve complicity in the moral evil of abortion, would legitimate abortion practices, and would provide incentives for abortions. Finally, it considers whether the donation model is appropriate for the transfer of human **fetal tissue** and whether the woman who chooses to have an abortion is the appropriate **donor** of the tissue.

L18 ANSWER 6 OF 21 MEDLINE on STN

ACCESSION NUMBER: 2000402190 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10904957  
TITLE: [Neural transplants en Parkinson disease: clinical results of 10 years of experience. Group of Neural Transplants of the CPH].  
Transplantes neurales en la enfermedad de Parkinson: resultados clinicos tras 10 anos de experiencia. Grupo de Trasplantes Neurales de la CPH.  
AUTHOR: Lopez-Lozano J J; Mata M; Bravo G  
CORPORATE SOURCE: Departamento de Neurologia, Universidad Autonoma de Madrid, Espana.. jlozano@cexp.cph.es  
SOURCE: Revista de neurologia, (2000 Jun 1-15) 30 (11) 1077-83.  
Journal code: 7706841. ISSN: 0210-0010.  
PUB. COUNTRY: Spain  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Spanish  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200008  
ENTRY DATE: Entered STN: 20000901  
Last Updated on STN: 20000901  
Entered Medline: 20000822

AB INTRODUCTION: At the end of the 1970s people considered the possibility that **transplants** might be useful to replace degenerate specific cell populations, **such** as the mesencephalic dopaminergic neurones in Parkinson's disease (PD). Since then this has become an experimental alternative treatment for patients with degenerative diseases. The history of **transplants** of catecholamine producing tissues within the brain of patients with PD started in 1985, when Backlund et al published the results of the first implants of autologous adrenal medulla in two patients with Parkinsonism. Since then, many patients throughout the world have benefited from the results obtained using this method. Two main types of tissue have been used in this method: autologous adrenal medulla and human foetal ventral mesencephalic tissue. DEVELOPMENT: In this paper we first review the clinical effects of the diverse types of **transplant** done to date. Then in the second part we give a summary of the clinical results obtained by our group with the different types of **transplant** carried out. We explain their evolution, original hypothesis and justify the reasons which led us to use three different types of **donor** material: autologous adrenal medulla, **fetal tissue** and adrenal medulla co-incubated with peripheral nerve. Then, after showing that the clinical improvement is different depending on the type of tissue **transplanted**, we comment on the probable reason for the improvement seen in patients with implants. CONCLUSION: The **transplantation** of nervous tissue seems to us to be no longer an experimental alternative for the treatment of PD but has become an effective, lasting treatment for patients with Parkinson's disease.

L18 ANSWER 7 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 2000260449 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10800655  
TITLE: Engineering hematopoietic grafts using elutriation and positive cell selection to reduce GVHD.  
AUTHOR: Noga S J  
CORPORATE SOURCE: Johns Hopkins Oncology Center, Baltimore, MD 21205, USA.  
CONTRACT NUMBER: CA 15396 (NCI)  
CA67787 (NCI)  
HL 46533 (NHLBI)  
SOURCE: Cancer treatment and research, (1999) 101 311-30. Ref: 60  
Journal code: 8008541. ISSN: 0927-3042.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, ACADEMIC)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200006  
ENTRY DATE: Entered STN: 20000714  
Last Updated on STN: 20000714  
Entered Medline: 20000630

AB A systematic approach to hematopoietic graft manipulation has minimized

several of the variables inherent to allogeneic BMT. Through this approach, we have been able to significantly impact on morbidity and quality of life following allogeneic **transplantation**. Acute and chronic GVHD, blood product and antibiotic usage, in patient hospitalization, acuity, costs and survival (especially in patients older than 40) have been improved. The HLA barrier still presents a formidable obstacle to achieving a more widespread use of this therapy. The complications encountered in HLA matched/TCD grafts occur with even greater magnitude in the HLA-mismatched or unrelated donor setting. Several centers are now engaged in studies using TCD grafts that are augmented with high doses of CD34+ cells to ensure engraftment while reducing the incidence of GVHD (50-53). Mobilized allogeneic PBSC appear to be an excellent source of stem cells for BMT (5,6). The earlier reports showed decreased rates of GVHD, despite having T cell burdens 10 times higher than those found in unmanipulated bone marrow. However, several of these centers now report an unacceptably high incidence of chronic GVHD (along with its attendant morbidity) following allogeneic PBSC **transplantation** (54-55). Initial results of TCD in these PBSC grafts using CD34+ selection are disappointing in that recipients developed unexpectedly high incidences of both acute and chronic GVHD (56). No doubt, significant differences exist between marrow and PBSC ancillary cell populations. For example, two laboratories now report the presence of natural suppressor cells in these allogeneic PBSC products in both mice (57) and humans (58). Thus, the same, step-wise approach would be expected to improve graft performance when using PBSC, cord blood, **fetal tissue**, xenografts or genetically engineered products as a stem cell source. Indeed, there are new reports of improved clinical outcome (especially in the incidence of GVHD) in the PMRD setting using both CD34+ selected (59) and sequential CD34+/CD2+ selected (60) PBSC grafts. It is hoped that future graft engineering approaches will be as **successful** as previous studies and will extend this form of therapy to an even larger patient population.

L18 ANSWER 8 OF 21 MEDLINE on STN  
 ACCESSION NUMBER: 1999439259 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 10511241  
 TITLE: Isolation and intracerebral grafting of nontransformed multipotential embryonic human CNS stem cells.  
 AUTHOR: Vescovi A L; Gritti A; Galli R; Parati E A  
 CORPORATE SOURCE: National Neurological Institute C. Besta, Milan, Italy.. vescovi@tin.it  
 SOURCE: Journal of neurotrauma, (1999 Aug) 16 (8) 689-93.  
 Journal code: 8811626. ISSN: 0897-7151.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199911  
 ENTRY DATE: Entered STN: 20000111  
 Last Updated on STN: 20000111  
 Entered Medline: 19991124

AB In this work, we show that the embryonic human brain contains multipotent central nervous system (CNS) stem cells, which may provide a continuous, standardized source of human neurons that could virtually eliminate the use of primary human fetal brain tissue for intracerebral **transplantation**. Multipotential stem cells can be isolated from the developing human CNS in a reproducible fashion and can be exponentially expanded for longer than 2 years. This allows for the establishment of continuous, nontransformed neural cell lines, which can be frozen and banked. By clonal analysis, reverse transcription polymerase chain reaction, and electrophysiological assay, we found that over **such** long-term culturing these cells retain both multipotentiality and an unchanged capacity for the generation of neuronal cells, and that they can be induced to differentiate into catecholaminergic neurons. Finally, when **transplanted** into the brain of adult rodents immunosuppressed by cyclosporin A, human CNS stem cells migrate away from the site of injection and differentiate into neurons and astrocytes. No tumor formation was ever observed. Aside from depending on scarce human neural **fetal tissue**, the use of human embryonic CNS stem cells for clinical neural **transplantation** should provide a reliable solution to some of the major problems that

pertain to this field, and should allow determination of the safety characteristics of the donor cells in terms of tumorigenicity, viability, sterility, and antigenic compatibility far in advance of the scheduled day of surgery.

L18 ANSWER 9 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 97176549 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9024088  
TITLE: Tissue distribution of transplanted fetal liver cells in the human fetal recipient.  
AUTHOR: Westgren M; Ek S; Bui T; Jansson B; Kjaeldgaard A; Markling L; Nennesmo I; Seiger A; Sarby B; Thornstrom S; Ringden O  
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Huddinge University Hospital, Sweden.  
SOURCE: American journal of obstetrics and gynecology, (1997 Jan) 176 (1 Pt 1) 49-53.  
Journal code: 0370476. ISSN: 0002-9378.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199703  
ENTRY DATE: Entered STN: 19970321  
Last Updated on STN: 19970321  
Entered Medline: 19970313

AB OBJECTIVE: Our purpose was to study the tissue distribution and concentrations of **transplanted** fetal liver cells in the human fetus. STUDY DESIGN: Radiolabeled indium 111 fetal liver cells were injected in vivo under ultrasonographic guidance into 10 normal fetuses (13 to 17 weeks of gestation) before a prostaglandin abortion. Six fetuses were injected intraperitoneally and four intracardially. Another two fetuses serving as controls were injected with indium-labeled maternal plasma. The fetuses were all alive, at least until 6 hours before expulsion. After expulsion the fetuses were dissected, and radioactivity was measured in various fetal tissues. Results for each tissue were expressed as percentages of the total injected dose. RESULTS: Significantly greater uptake of fetal liver cells in the liver, spleen, thymus, kidney, lung, and placenta was obtained with intracardiac than with intraperitoneal injection. Skeletal uptake did not differ in relation to mode of administration. With intracardiac injection uptake was greater in such parenchymal organs as the liver, spleen, and thymus (4.9%, 4.0%, and 3.9%, respectively). Uptake in the rib, clavicle, humerus, and sternum was 2.7%, 1.8%, 2.1%, and 1.1%, respectively. Placental uptake was 0.1%. The intracardiac route yielded a higher concentration of cells in different fetal organs than did injection of only radiolabeled maternal plasma, suggesting an active uptake of cells in different fetal hematopoietic organs. CONCLUSION: The mode of administration of fetal liver cells seems to be a major determinant of donor cell concentration in the **transplanted** human fetus and may be a significant determinant of the rate of **successful** engraftment.

L18 ANSWER 10 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 97153383 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9000673  
TITLE: Discordant xenogeneic neonatal thymic transplantation can induce donor-specific tolerance.  
AUTHOR: Khan A; Sergio J J; Zhao Y; Pearson D A; Sachs D H; Sykes M  
CORPORATE SOURCE: Transplantation Biology Research Center, Massachusetts General Hospital/Harvard Medical School, Boston 02129, USA.  
CONTRACT NUMBER: 1K11AI01261-01 (NIAID)  
SOURCE: Transplantation, (1997 Jan 15) 63 (1) 124-31.  
Journal code: 0132144. ISSN: 0041-1337.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199702  
ENTRY DATE: Entered STN: 19970227  
Last Updated on STN: 19970227  
Entered Medline: 19970213

AB The limited supply of human organs for **transplantation** necessitates the development of methods leading to acceptance of xenografts. To avoid the hazards of the high-dose chronic immunosuppressive pharmacotherapy which would otherwise be required for **successful** xenografting, it would be desirable to induce permanent tolerance to xenogeneic **donors**. We have recently demonstrated that xenogeneic **donor**-specific tolerance can be induced by **transplanting** fetal pig thymic and hematopoietic tissue into thymectomized, T cell-depleted, and natural killer-cell-depleted mice, or into natural killer cell-depleted nude mice. We have now extended these studies by replacing **fetal tissue** with neonatal pig thymic and hematopoietic tissue, and by examining the in vivo responses of reconstituted mice to pig skin grafts. Neonatal tissue was studied because it might be more practicable than **fetal tissue** for the purpose of **transplantation** to primates. BALB/c nu/nu mice **transplanted** with neonatal (<24-hr-old) pig thymus and spleen fragments developed circulating mouse CD4+ cells. The pig thymus grafts were necessary for mouse T-cell development, as CD4 recovery did not occur in recipients of neonatal pig splenic tissue alone. The CD4+ cells that developed included Vbeta8.1/2+ T cells in similar proportions as in BALB/c mice, and Vbeta11+ and Vbeta5+ CD4 T cells were deleted almost as completely as in normal BALB/c mice. This deletion was detected among CD4 single-positive graft thymocytes. In 9 of 12 evaluable animals, mixed lymphocyte responses demonstrated tolerance to **donor**-type pig SLA antigens, with responsiveness to alloantigens and/or third-party pig xenoantigens. Furthermore, grafting of neonatal pig thymus conferred the ability to reject allogeneic mouse skin in 7 of 10 animals. In addition, 7 of 10 animals accepted paternal (**donor** SLA-matched) skin (median survival time [MST] > 100 days), whereas 4 of 4 animals rejected third-party SLA-mismatched pig skin (MST=40.5 days). We conclude that neonatal pig thymi **transplanted** to BALB/c nu/nu mice can support the development of mouse CD4+ cells that are functional and specifically tolerant to **donor**-type pig antigens.

L18 ANSWER 11 OF 21 MEDLINE on STN  
 ACCESSION NUMBER: 96393740 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 8800513  
 TITLE: A mathematical model for the estimation of human embryonic and fetal age.  
 AUTHOR: Evtouchenko L; Studer L; Spenger C; Dreher E; Seiler R W  
 CORPORATE SOURCE: Department of Neurosurgery, University of Bern, Inselspital, Switzerland.  
 SOURCE: Cell transplantation, (1996 Jul-Aug) 5 (4) 453-64.  
 Journal code: 9208854. ISSN: 0963-6897.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199702  
 ENTRY DATE: Entered STN: 19970305  
 Last Updated on STN: 19970305  
 Entered Medline: 19970220

AB Precise determination of **donor** age in human embryonic and **fetal tissue** is crucial for cell **transplantation** due to the existence of distinct time windows within which **successful** grafting is possible. This study demonstrates that between 4-12 wk postconception embryonic and fetal age can be estimated based on various morphometric parameters measured on a routine basis in **suction** abortion material. The greatest length, the neck-rump length, the foot length, and the proximal and distal arm and leg length were correlated with the anamnestic and ultrasonographically estimated age. Multivariate regression analyses showed a linear correlation between age and the logarithmic value of the various morphometric parameters. The best correlation was found for a mathematical model combining the limb parameters ( $r = 0.904$ ;  $p < 0.001$ ;  $n = 37$ ). A prospective follow-up study ( $n = 40$ ) was carried out to test the validity of the mathematical model. A high correlation was found between the calculated age and the estimated age based on anamnestic data ( $r = 0.749$ ,  $p < 0.001$ ). Outliers due to errors in the anamnestic data were readily identified by comparing anamnestic with calculated age. This method allows determination of embryonic and fetal age within and beyond the age group of the Carnegie

classification and may, therefore, be useful for the needs of experimental and clinical cell **transplantation**.

L18 ANSWER 12 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 96350807 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8714776  
TITLE: Development of the human striatum: implications for fetal striatal transplantation in the treatment of Huntington's disease.  
AUTHOR: Freeman T B; Sanberg P R; Isacson O  
CORPORATE SOURCE: Department of Pharmacology and Experimental Therapeutics, University of South Florida, Tampa 33606, USA.  
CONTRACT NUMBER: NS29178 (NINDS)  
SOURCE: Cell transplantation, (1995 Nov-Dec) 4 (6) 539-45. Ref: 61  
Journal code: 9208854. ISSN: 0963-6897.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199610  
ENTRY DATE: Entered STN: 19961025  
Last Updated on STN: 20000303  
Entered Medline: 19961017

AB Fetal neural **transplantation** has recently been demonstrated to ameliorate motor and other behavioral deficits in animals models of Huntington's disease, and reconstruct many of the damaged striatal circuits. However, there has been significant variability in the histological appearance of these grafts, most likely related to differences of the regions of dissection of the **donor** tissue. Selective dissection and **transplantation** of the lateral ventricular eminence in rodents has resulted in grafts consisting of primarily striatal-like tissue. This data, combined with data from our own and other laboratories has led to a description of the development of human striatum, with a particular emphasis on the relevance of human striatal development to the field of **fetal tissue transplantation** for the treatment of Huntington's disease. If the goal of **transplantation** is to graft GABAergic striatal projection neurons, it is our impression that optimal grafting results will occur when **transplants** are derived from the lateral ventricular eminence and the lateral aspect of the body of the ventricular eminence anterior to the foramen of Monro. Optimal results are likely to occur when **donor** ages range from Stage 19 to 23, with possible graft **success** when **donor** age extends to as late as postovulatory week 22.

L18 ANSWER 13 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 94309086 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8035438  
TITLE: Attitudes of women to fetal tissue research.  
AUTHOR: Anderson F; Glasier A; Ross J; Baird D T  
CORPORATE SOURCE: University of Edinburgh's Department of Obstetrics and Gynaecology.  
SOURCE: Journal of medical ethics, (1994 Mar) 20 (1) 36-40.  
Journal code: 7513619. ISSN: 0306-6800.  
Report No.: KIE-43400.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Bioethics; Priority Journals  
ENTRY MONTH: 199408  
ENTRY DATE: Entered STN: 19940825  
Last Updated on STN: 20030318  
Entered Medline: 19940815

AB The use of human **fetal tissue** for scientific research has enormous potential but is subject to government legislation. In the United Kingdom the Polkinghorne Committee's guidelines were accepted by the Department of Health in 1990. These guidelines set out to protect women undergoing termination of pregnancy from exploitation but in so doing may significantly restrict potential research. Although the

committee took evidence from a wide variety of experts they did not seek the views of the general public. We asked 108 women about to have a therapeutic abortion; 167 women who had had a pregnancy terminated in the past, and 419 women who had never had an abortion, their views on research using human **fetal tissue**. Regardless of their past experiences the women were overwhelmingly in favour of research using **fetal tissue** (94 per cent). They made little distinction between basic research and research with obvious clinical relevance and supported the concept of using **transplanted fetal tissue** for the treatment of adult disease such as Parkinsonism. Women about to undergo an abortion were significantly more likely ( $p < 0.001$ ) to approve of all types of research including that aimed at improving methods of abortion and research using live fetuses in **utero**.

L18 ANSWER 14 OF 21 MEDLINE on STN  
 ACCESSION NUMBER: 91294243 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 2066374  
 TITLE: Cellular replacement therapy for neurologic disorders: potential of genetically engineered cells.  
 AUTHOR: Chen L S; Ray J; Fisher L J; Kawaja M D; Schinstine M; Kang U J; Gage F H  
 CORPORATE SOURCE: Department of Neurosciences, University of California, San Diego, La Jolla 92093.  
 CONTRACT NUMBER: NS01411 (NINDS)  
 SOURCE: Journal of cellular biochemistry, (1991 Mar) 45 (3) 252-7.  
 Ref: 32  
 Journal code: 8205768. ISSN: 0730-2312.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199108  
 ENTRY DATE: Entered STN: 19910901  
 Last Updated on STN: 19970203  
 Entered Medline: 19910809

AB Neural **transplantation**, a mode of cellular replacement, has been used as a therapeutic trial for Parkinson's disease. Studies indicate that tonic release of the metabolites from the graft that can be utilized by the host brain, is likely to be the major mechanism responsible for the therapeutic effect. The use of **fetal tissue** is complicated by ethical controversy and immunological incompatibility. Autografting adult tissue has not been **successful** mainly due to poor survival. Genetically engineered cells are promising alternative sources of **donor** cells. We have investigated the potential of primary skin fibroblasts as **donor** cells for intracerebral grafting. Primary skin fibroblasts survive in the brain and remain in situ. A number of genes (nerve growth factor, tyrosine hydroxylase, glutamic acid decarboxylase, and choline acetyltransferase) have been **successfully** introduced and expressed in the primary fibroblasts. The L-dopa-secreting primary fibroblasts exhibited a behavioral effect in a rat model of Parkinson's disease up to 8 weeks after being grafted into denervated striatum. Factors that can maximize gene transfer, transgene expression, and fibroblast survival in the brain make up the future direction of investigation.

L18 ANSWER 15 OF 21 MEDLINE on STN  
 ACCESSION NUMBER: 89334222 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 2667429  
 TITLE: [Prenatal diagnosis of severe and hereditary immune deficiencies].  
 Diagnostic prenatal des deficits immunitaires graves et hereditaires.  
 AUTHOR: Durandy A; Griscelli C  
 SOURCE: Annales de pediatrie, (1989 Jun) 36 (6) 403-7. Ref: 14  
 Journal code: 2984696R. ISSN: 0066-2097.  
 PUB. COUNTRY: France  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: French  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198908  
ENTRY DATE: Entered STN: 19900309  
Last Updated on STN: 19900309  
Entered Medline: 19890830

AB Antenatal diagnosis is now available for most severe inherited immune deficiencies. Several techniques are used: the development of methods for sampling fetal tissue as soon as the tenth week of gestation has made possible the antenatal diagnosis of immune deficiencies associated with detectable enzyme defects, and, in combination with recent molecular biology techniques, can be expected to allow early identification of severe combined immune deficiencies due to the absence of T lymphocyte precursors, agammaglobulinemia, and some instances of X-linked chronic granulomatous disease. A great number of immune deficiencies can be identified by direct studies of fetal lymphocytes or polymorphonuclear leukocytes in fetal blood sampled by fetoscopy at the twentieth week of gestation. Fetal blood studies combined with skin biopsy examination allows the diagnosis of immune defects associated with partial albinism such as Chediak-Higashi disease. No reliable antenatal diagnostic method is as yet available for two severe diseases: Wiskott-Aldrich syndrome, that can be expected to become detectable in utero using molecular biology techniques, and ataxia-telangiectasia. Antenatal diagnosis of a severe immune deficiency does not necessarily indicate termination of the pregnancy as in some cases, such as severe combined immune deficiencies, HLA-identical bone marrow transplantation at birth or in utero is permanently successful in over 90% of cases.

L18 ANSWER 16 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 88314195 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 3044989  
TITLE: Bone marrow transplantation in the treatment of severe immunodeficiencies: possibilities and problems.  
AUTHOR: Vossen J M  
CORPORATE SOURCE: Department of Pediatrics, University Hospital Leiden, The Netherlands.  
SOURCE: Immunological investigations, (1988 Apr) 17 (2) 135-46.  
Ref: 20  
Journal code: 8504629. ISSN: 0882-0139.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198809  
ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 19900308.  
Entered Medline: 19880929

AB Infants and children suffering from severe primary immunodeficiencies may be cured by bone marrow transplantation from a healthy donor. Data obtained in 14 European centers show that about 60% of the patients are surviving disease-free, if they were grafted with bone marrow cells from an HLA-identical related donor. Results of transplantation of T-cell depleted bone marrow from an HLA-haploidentical related donor were also excellent in infants with severe combined immunodeficiency, with 60% recovery. This therapy is superior to transplantation of fetal tissues. HLA-haploidentical T-cell depleted marrow transplantation for other severe immunodeficiencies was less successful. This was mainly due to failure of engraftment, despite intensive conditioning of the recipient, and to infectious complications e.g. by reactivation of latently present viruses.

L18 ANSWER 17 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 88127912 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 3324405  
TITLE: Fetal tissue transplantation, bone marrow transplantation and prospective gene therapy in severe immunodeficiencies



and enzyme deficiencies.  
AUTHOR: Touraine J L; Roncarolo M G; Royo C; Touraine F  
CORPORATE SOURCE: Transplantation and Immunobiology Unit, Hopital Edouard  
Herriot, Lyon, France.  
SOURCE: Thymus, (1987) 10 (1-2) 75-87.  
Journal code: 8009032. ISSN: 0165-6090.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198803  
ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 19900308  
Entered Medline: 19880304

AB The successful development of fetal tissue transplantation has resulted in therapeutical solutions for patients with a variety of diseases. Fetal liver transplants as well as bone marrow transplants, can completely cure patients with severe combined immunodeficiency disease. These transplants can also be applied to treat other types of immunodeficiency, hemopathies, and inborn errors of metabolism, in association with immunosuppressive therapy. Despite complete HLA incompatibility between transplanted stem cells and host cells, functional activities of donor-derived T-lymphocytes are not restricted. In severe forms of Di George syndrome, immunological reconstitution can be obtained by fetal thymus transplantation. It is expected that, in the near future, pure stem cell transplants and gene transplants will develop and will provide remarkable solutions for the therapy of a large number of diseases.

L18 ANSWER 18 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 87063073 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2878238  
TITLE: Organ procurement for children: the anencephalic fetus as donor.  
AUTHOR: Harrison M R  
SOURCE: Lancet, (1986 Dec 13) 2 (8520) 1383-6.  
Journal code: 2985213R. ISSN: 0140-6736.  
Report No.: KIE-23912.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Bioethics; Priority Journals  
ENTRY MONTH: 198701  
ENTRY DATE: Entered STN: 19900302  
Last Updated on STN: 20030318  
Entered Medline: 19870116

AB A member of a medical center fetal treatment program and division of pediatric surgery discusses the technical feasibility and unique suitability of fetal tissue and organ transplants for treatment of diseases and congenital defects in children. He argues that anencephalic fetuses would be ideal donors. Although some maintain that the anencephalic newborn is incapable of achieving personhood because it lacks the forebrain necessary for characteristic human activity, Harrison rejects using this claim because of the controversy concerning personhood, the potential for lack of respect for the fetus and its parents, and the possibility that less severely handicapped fetuses might be denied personhood. He proposes that the anencephalic fetus be considered a dying person because of clearly definable brain absence, and that such a fetus be recognized as brain dead for medicolegal purposes. The family could then be approached concerning donation.

L18 ANSWER 19 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 84137223 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 6366090  
TITLE: HLA antigens in choriocarcinoma.  
AUTHOR: Sasagawa M; Suzuki T; Kajino T; Ohno M; Kanazawa K; Takeuchi S  
SOURCE: Nippon Sanka Fujinka Gakkai zasshi, (1984 Jan) 36 (1) 81-4.

Journal code: 7505749. ISSN: 0300-9165.

PUB. COUNTRY: Japan  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Japanese  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198403  
ENTRY DATE: Entered STN: 19900319  
Last Updated on STN: 19900319  
Entered Medline: 19840326

AB Choriocarcinoma can be regarded as **transplanted** cancer, because its origin is in trophoblast which is **fetal tissue**. It is of interest whether HLA antigens are expressed on choriocarcinoma cells or not, since HLA antigens may play an important role if the patient's body could recognize choriocarcinoma as "not self" and initiate its immune response. In this report choriocarcinoma tissue in the uterus, obtained after hysterectomy, is stained by an indirect immunofluorescence technique using monoclonal antibodies to HLA-A,B,C and HLA-DR. We believe this is the first immunohistological study in which choriocarcinoma in **utero** is available for study and monoclonal antibodies to HLA antigens are applied. In the staining of HLA-A,B,C, and of HLA-DR, host cells, **such** as myometrial cells, show positive staining but choriocarcinoma cells show negative staining. It is thought that choriocarcinoma cells are viable and show negative staining of HLA antigens, on the basis of finding following HE staining and hCG staining using anti-hCG antibody and the clinical remarks of the patient **such** as her high urinary hCG titer before operation and no history of chemotherapy. These results agree with those of previous studies about HLA antigens on choriocarcinoma cell lines.

L18 ANSWER 20 OF 21 MEDLINE on STN

ACCESSION NUMBER: 83216183 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 6854669  
TITLE: Growth, differentiation, and viability of fetal rat cortical and spinal cord implants into adult rat spinal cord.

AUTHOR: Patel U; Bernstein J J  
SOURCE: Journal of neuroscience research, (1983) 9 (3) 303-10.  
Journal code: 7600111. ISSN: 0360-4012.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198307  
ENTRY DATE: Entered STN: 19900319  
Last Updated on STN: 19900319  
Entered Medline: 19830729

AB **Successful transplantation** of the fetal brain into adult host brain has been accomplished. These studies explore the growth, differentiation, and viability of E11, E12, and E15 rat fetal cortex and fetal spinal cord implantation into the spinal cord of adult rats (**donor** and host, Sprague-Dawley). Under deep Chloropent anesthesia, 70 rats had 1-mm cubes of fetal cortex inserted with pressure or by stylus injection subpially between the dorsal horn and dorsal column (left side), or implantation of whole segments of fetal spinal cord. Animals were prepared for light microscopy 14 and 21 days and 1, 2, and 3 months later. Implants by both **fetal tissues** had a 69% survival rate. The younger the fetal implant the higher the **success** of the implant (E11 greater than E15). The diameter of fetal spinal cord implants reached the diameter of control postnatal animals after 30 days. The implants not only increased in mass (up to 7-fold in some cases) but differentiated and matured (apolar, unipolar, bipolar, and multipolar) neurons were observed one to three months postimplantation. By 30 days postimplantation, fetal neurons had large, often crenated nuclei, with a large single prominent nucleolus. The most **successful** implants were the young E11 fetal spinal cord into the adult host spinal cord. These implants represent an initial **successful transplantation** of fetal spinal cord into adult spinal cord.

L18 ANSWER 21 OF 21 MEDLINE on STN  
ACCESSION NUMBER: 82130188 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7036455  
 TITLE: Sex-associated differences in the immune response against fetal major histocompatibility antigens.  
 AUTHOR: Tartakovsky B; De Baetselier P; Feldman M; Segal S  
 SOURCE: Transplantation, (1981 Nov) 32 (5) 395-7.  
 Journal code: 0132144. ISSN: 0041-1337.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198204  
 ENTRY DATE: Entered STN: 19900317  
 Last Updated on STN: 19900317  
 Entered Medline: 19820420

AB Alloantibodies against H-2b and H-2k haplotypes were produced in C57BL/6J and C3H female and male mice in response to **transplantation** of F1 **fetal tissue** (bone) or adult F1 cells (spleen). Testing IgG1 and IgG2 antibodies by means of the fluorescence-activated cell sorter (FACS II), we found no differences between males and females in the isotype content of antisera produced against spleen cells from adult **donors**. In contrast, striking sex-associated differences were found in the isotypes produced against fetal allografts: females produced much more IgG1 than males, although they produced comparable amounts of IgG2. Hence, it appears that females differ from males in their humoral alloreactivity against major histocompatibility complex (MHC) gene products expressed on fetal cells. **Such** MHC antigens expressed on **fetal tissues** seem to generate different immune signals than the MHC antigens expressed on adult cells. These observations might be of relevance to the biological role played by the IgG1 alloantibodies produced during pregnancy against the MHC alloantigens of the fetus.

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(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
 L2 146532 S IN UTERO OR DONOR  
 L3 59250 S PERCUTAN?  
 L4 2 S L1 (S) L2 (S) 3  
 L5 0 S L1 (S) L2 (S) L3  
 L6 60 S L1 (S) L2  
 L7 23472 S INCISION  
 L8 0 S L1 (S) L2 (S) L7  
 L9 354581 S TRANSPLANT?  
 L10 14 S L1 (S) L2 (S) L9  
 L11 1197155 S SUCTION OR VACUUM OR SUC?  
 L12 1 S L1 (S) L2 (S) L9 (S) L11  
 L13 1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?  
 L14 1 S L1 (S) L2 (S) L9 (S) L13  
 L15 247721 S ?CUTAN?  
 L16 0 S L1 (S) L2 (S) L9 (S) L15  
 L17 0 S L1 (L) L2 (L) L9 (L) L15  
 L18 21 S L1 (L) L2 (L) L9 (L) L13

=> s 11 (1) 115

L19 64 L1 (L) L15

=> s 11 (1) 115 (1) 119

L20 64 L1 (L) L15 (L) L19

=> s 11 (1) 115 (1) 119 (1) 113

L21 13 L1 (L) L15 (L) L19 (L) L13

=> d 1-13 ibib abs

L21 ANSWER 1 OF 13 MEDLINE on STN  
 ACCESSION NUMBER: 2004087750 IN-PROCESS  
 DOCUMENT NUMBER: PubMed ID: 14977357

TITLE: Low iron diet and parenteral cadmium exposure in pregnant rats: the effects on trace elements and fetal viability.

AUTHOR: Piasek Martina; Blanusa Maja; Kostial Krista; Laskey John W

CORPORATE SOURCE: Mineral Metabolism Unit, Institute for Medical Research and Occupational Health, P.O. Box 291, HR-10001 Zagreb, Republic of Croatia.. mpiasek@imi.hr

SOURCE: Biometals : an international journal on the role of metal ions in biology, biochemistry, and medicine, (2004 Feb) 17 (1) 1-14.

Journal code: 9208478. ISSN: 0966-0844.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals

ENTRY DATE: Entered STN: 20040224

Last Updated on STN: 20040224

AB The effects of latent iron deficiency combined with parenteral subchronic or acute cadmium exposure during pregnancy on maternal and fetal tissue distribution of cadmium, iron and zinc, and on fetal viability were evaluated. Timed-pregnant Sprague-Dawley rats were fed on semisynthetic test diets with either high iron (240 mg kg) or low iron (10 mg kg), and concomitantly exposed to 0, 3 or 5 mg cadmium (as anhydrous CdCl<sub>2</sub>) per kilogram body weight. Animals were exposed to cadmium from gestation day 1 through 19 by subcutaneously implanted mini pumps (Subchronic exposure) or on gestation day 15 by a single subcutaneous injection (Acute exposure). All rats were killed on gestation day 19. Blood samples, selected organs and fetuses were removed and prepared for element analyses by atomic absorption spectrometry. Low iron diet caused decreases in maternal body weight, maternal and fetal liver weights, placental weights and tissue iron concentrations. By cadmium exposure, both subchronic and acute, tissue cadmium concentrations were increased and the increase was dose-related, maternal liver and kidney zinc concentrations were increased, and fetal zinc concentration was decreased. Cadmium concentration in maternal liver was additionally increased by low iron diet. Acute cadmium exposure caused lower maternal body and organ weights, high fetal mortality, and decreased fetal weights of survivors. In conclusion, parenteral cadmium exposure during pregnancy causes perturbations in essential elements in maternal and fetal compartments. Acute cadmium exposure in the last trimester of gestation poses a risk for fetal viability especially when combined with low iron in maternal diet.

L21 ANSWER 2 OF 13 MEDLINE on STN

ACCESSION NUMBER: 2003121718 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12635741

TITLE: Can human fetal cortical brain tissue transplant (up to 20 weeks) sustain its metabolic and oxygen requirements in a heterotopic site outside the brain? A study of 12 volunteers with Parkinson's disease.

AUTHOR: Bhattacharya N; Chhetri M K; Mukherjee K L; Ghosh A Baran; Samanta B Krishna; Mitra R; Bhattacharya M; Bhattacharya S; Bandopadhyaya T

CORPORATE SOURCE: Bijoygarh State Hospital, Calcutta, India.

SOURCE: Clinical and experimental obstetrics & gynecology, (2002) 29 (4) 259-66.

Journal code: 7802110. ISSN: 0390-6663.

PUB. COUNTRY: Italy

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200305

ENTRY DATE: Entered STN: 20030316

Last Updated on STN: 20030507

Entered Medline: 20030506

AB BACKGROUND: Neural and stem cell transplantation is emerging as a potential treatment for neurodegenerative diseases from Parkinson's to Huntington's disease. Stereotactic placement of dopaminergic neurons in the caudate-putamen (striatum), is being attempted in centers of excellence and has proved to be beneficial. Basic research using cell transplantation indicates that structural development mechanisms seen in immature brains, i.e., fetal brains, can also function in the adult brain.

The adult brain consumes 15% of the resting cardiac output for its metabolic needs. While most human tissues can sustain an anaerobic assault for a few minutes up to 30 minutes, a sudden total lack of oxygen supply to the brain cells in an adult will render the person unconscious within five to ten seconds. Our team has been working on the problem of human fetal tissue response to antigenic assault for the last two decades. In the present series, 12 patients with prolonged histories of Parkinsonism, who were not responding to anti-Parkinsonian drugs, and could not afford costly stereotactic surgery or deep brain stimulation and other modalities of recent Parkinson's disease treatment, were enrolled in the study. MATERIALS AND METHOD: After obtaining proper informed consents from the patients or their guardians and from the multidisciplinary ethical committee, the patients, varying in age from 45 to 75 years and suffering for many years with Parkinsonism, were enrolled in the heterotopic brain tissue transplant programme. We followed standard antiseptic, aseptic and premedication protocols, after selecting a proposed site of transplantation of the brain in the axillary fold of the skin, under local infiltration anaesthesia. In an adjacent OR, a fetus was collected from a consenting patient undergoing hysterotomy and ligation (before 20 weeks), under general anaesthesia. Within a minute of hysterotomy, the fetal brain tissue was dissected, and under the guidance of the operative microscope, 1 g of fetal cortical brain tissue was dissected and weighed in an electronic machine. The tissue was collected from around 1 cm of the frontal opercula of the developing human fetal brain and grafted in the already dissected and prepared subcutaneous site in the axilla and the skin was closed. Hematological parameters (Hgb; total count, Tc; differential count, Dc; erythrocyte sedimentation rate, ESR) were estimated sequentially up to one month. A small portion of the transplanted tissue was retrieved after one to two months, and a serial histological study was done along with a clinical assessment of the disease condition as per the specifications of the Unified Parkinson's Disease Rating Scale. The results were matched with the pre-transplant ratings of the individual cases. Presenting dyskinesia was also rated (0-4), on the basis of objective criteria assessment like walking, putting on a coat, lifting a cup to drink, etc. RESULTS AND ANALYSIS: Initially 30 patients suffering from advanced Parkinson's disease (PD) were approached after getting the necessary clearance from the institutional multidisciplinary ethical committee; however, we have been able to arrange transplantation in only 12 cases so far. These patients were evaluated at the pre- and one month post-transplant period by the Unified Parkinson's Disease Rating Scale (0-108) and the minimum score was 40 in the motor portion of the unified scale at the pre-transplant state. Evaluation of the patients after one month revealed mild improvement of the pre-transplant scoring (up to 33.3%) in 41.6% of the cases, and moderate improvement (up to 66.6%) in another 41.6% of the cases. While 16.8% of the cases did not show any improvement from the basal score, i.e., the pre-transplant score, there was a definite sense of well being and rise in weight (2-4 pounds) noted in each case and there was also a reduction of the L-Dopa dosage in 75% of the cases. There was also a 58.3% improvement in the bradykinesia scoring from the pre-transplant level. What is intriguing is the survival, growth and proliferation of the grafted fetal brain tissue in the HLA- and sex-randomized adult axilla without any immunosuppressive support. Not a single histological study of the fetal brain tissues after removal from the axilla showed any signs of graft vs. host or inflammatory reaction (Figures 1-9) but there were features of growth of the transplanted cortical brain tissue along with its different components like neurogenesis, gliogenesis, early neovascularisation and angiogenesis, etc. There was also no systemic leucocytosis or lymphocytosis. DISCUSSION AND CONCLUSION: Histological evidence at the transplanted tissue site suggests that fetal cortical brain tissue can sustain life in sex-randomized, HLA-randomized adult hosts, without the support of immuno-suppressive drugs and the tacit support of the blood-CSF and blood-brain barrier and other specific requirements of adult brain cells in the skull. Whether the clinical improvement in PD is transient or long lasting is presently under investigation along with basic questions like, is it due to transplanted fetal dopaminergic or non-dopaminergic neurons or is it the growth factors and the cytokine mediated hitherto unknown reactions causing the clinical improvement.

ACCESSION NUMBER: 2003012687 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12519043  
TITLE: Human fetal adrenal transplant: a possible role in relieving intractable pain in advanced rheumatoid arthritis.  
AUTHOR: Bhattacharya N; Chhetri M K; Mukherjee K L; Das S Prasad; Mukherjee A; Bhattacharya M; Bhattacharya S  
CORPORATE SOURCE: Bijoygarh State Hospital, Calcutta, India.  
SOURCE: Clinical and experimental obstetrics & gynecology, (2002) 29 (3) 197-206.  
Journal code: 7802110. ISSN: 0390-6663.  
PUB. COUNTRY: Italy  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200304  
ENTRY DATE: Entered STN: 20030110  
Last Updated on STN: 20030404  
Entered Medline: 20030403

AB BACKGROUND: The art of transplant surgery has gone a long way in establishing itself as an important discipline in medicine with the support of molecular biology, immunology, biochemistry, etc., as the ultimate treatment for the restoration of function of a failing organ. With the progressive increase in the life expectancy of human beings, there is an increasing discrepancy in the demand and supply of organ grafts. A less efficient alternative could be synthetic or mechanical grafts. Nucleated cell therapy, that is, cellular transplant, is a promising new area of study with its proven efficacy in neuro-degenerative disorders, hematopoietic disorders, diabetes and trauma-induced tissue loss, to name a few. Human fetal cell/tissue with its intrinsic hypo-antigenic advantage (up to 20 weeks of study), could be an interesting area of cellular/tissue transplant. Our research group has earlier reported on the safe use of umbilical cord whole blood and the **successful** transplant of a human fetal lung, heart, pancreas, liver, thymus, in an artificially prepared vascular **subcutaneous** axillary fold in which there was no feature of hyper-acute, acute or chronic rejection of the graft in HLA- and sex-randomized adult recipients, without concomitant immunosuppressives or radiation of the host to potentiate the survival of the fetal graft (within 20 weeks of gestation) within the lowest observation period of one month. The present study was aimed at examining the role of developing fetal adrenal transplants for patients with rheumatoid arthritis and severe pain due to involvement of inflammatory and neuropathic components. MATERIALS AND METHOD: Ten cases were enrolled in the present study after thorough informed consent and approval by the ethical committee of the institute. The age of the patients varied from 50 to 76 years and the group was comprised of three males and seven females. The age of the adrenal grafts varied from 16 to 20 weeks and these were collected from mothers admitted for hysterotomy and ligation. These long-standing rheumatoid patients (suffering for five to 15 years), presented with at least four of the seven 1987 revised criteria of the American College of Rheumatology for diagnosis of rheumatoid arthritis. A 2.5 cm long and 2 cm deep tissue space was dissected and prepared in each transplant recipient at the axilla using diathermy and knife after infiltrating the site with one percent lignocaine solution. The tissue collected from the consenting mother undergoing hysterotomy and ligation was inserted into this site, and the site was closed with 00 atraumatic vicryl. All necessary pre- and postoperative surgical precautions were taken to prevent infections. Sequential total count and differential count of leucocytes were undertaken to analyze the impact of the transplant on the host. After one month, a part of the transplanted **fetal tissue** was recovered for histological staining to examine whether there was any graft versus host reaction. RESULTS AND ANALYSIS: All ten patients tolerated the transplant procedure well. There was no fever, intractable pain or any other specific serious side-effect which could justify the **removal** of the transplant before one month. There was no discharge from the incision site and the healing of the scar was by and large normal. There was no unusual leucocytosis, lymphocytosis and the retrieved graft tissue did not suggest transplant rejection. However, there was definite pain relief, reduction in swelling and improvement of mobility of varying degree in a majority of the patients which was

perceivable from the 15th day onwards. There was also a sense of well being (in 80%) and a gain in weight of three pounds or more (in 70%) among the fetal transplant recipients. **DISCUSSION AND CONCLUSION:** To understand the underlying mechanism, in case of pregnancy immunotolerance, we are of the opinion that emphasis should be placed on the role of non-specific and non-cytopathic blocking antibodies produced during pregnancy. The hypo-antigenicity of the developing human fetal system may possibly contribute to the production of this blocking antibody during pregnancy, and thus may play a role in the lack of recognition by the host's HLA system. This behaviour of the developing human **fetal tissue** provides some advantages over adult tissue for fetal cell/tissue transplantation purposes. The relief of pain, inflammation and restoration of mobility may be due to the effect of the transplanted adrenal graft, with the medullary component contributing to endorphin-like substance liberation and the cortical component contributing to glucocorticoid synthesis.

L21 ANSWER 4 OF 13 MEDLINE on STN  
 ACCESSION NUMBER: 2002107433 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11838747  
 TITLE: Fetal tissue/organ transplant in HLA-randomized adult vascular subcutaneous axillary folds: preliminary report of 14 patients.  
 AUTHOR: Bhattacharya N  
 CORPORATE SOURCE: Principal Investigator of the Project on Fetal Tissue Transplant in Adult Health and Disease, and Surgeon-Superintendent, Bijovygarh State Hospital, Calcutta, India.  
 SOURCE: Clinical and experimental obstetrics & gynecology, (2001) 28 (4) 233-9.  
 Journal code: 7802110. ISSN: 0390-6663.  
 PUB. COUNTRY: Italy  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200207  
 ENTRY DATE: Entered STN: 20020213  
 Last Updated on STN: 20020731  
 Entered Medline: 20020730

AB **BACKGROUND:** In the year 1902, the first **successful** experimental organ transplant, i.e., an autotransplant of a dog's kidney from its normal position to the vessels of the neck, which resulted in some urine flow, was performed in the Vienna Physiology Institute under the direction of Hofrath Exner by Dr. Emerich Ullman (1861-1937). Since then, the art of transplant surgery has come a long way in establishing itself as an important discipline with the support disciplines of immunology, molecular biology, etc., for the restoration of a failing organ. Today there is a major discrepancy in the demand and supply of organ grafts. The aim of the present study is to see whether fetal organ and tissue, with its intrinsic advantages of hypo-antigenicity, can survive in a HLA and sex-randomized host in a surgically prepared vascular **subcutaneous** axillary fold, without any immunosuppressive support. We have earlier reported two cases of fetal thymic transplant, collected from consenting mothers undergoing hysterotomy and ligation. **MATERIALS AND METHODS:** Fourteen cases were recruited for the present study after thorough informed consent and approval by the Ethical Committee of the Project. Of these, five patients were suffering from advanced cancer, three from diabetic gangrene, three from ischaemic heart disease and three from rheumatoid arthritis, liver abscess and disc prolapse. The ages of the patients varied from 39 to 82 years. Six fetal thymuses, three fetal liver tissues, three fetal cardiac tissues, one fetal pancreas and one fetal lung tissue were transplanted. All the fetuses were dissected and the selected tissues/organs were transplanted within one to three minutes after collecting them from the consenting mothers undergoing hysterotomy and ligation. The **fetal tissue** graft was placed in a surgically prepared **subcutaneous** vascular axillary fold, 2x1 cm, under local anaesthesia in the consenting adult recipient. Sequential Hb, Tc, Dc, ESR were done to see the impact of the transplant on the host system. After one month, the transplanted **fetal tissue** was taken out by an elliptical incision and the tissue was processed for histological staining. **RESULTS AND ANALYSIS:** All the 14 patients

tolerated the transplant procedure well. There was no fever, intractable pain or any other specific serious side-effect justifying **removal** of the transplant earlier. There was no discharge from the incision site and the healing and scar were by and large normal. There was no unusual leucocytosis or lymphocytosis. The serial histological study did not suggest features of transplant rejection. **DISCUSSION AND CONCLUSION:** Pregnancy and neoplasm are two outstanding examples of natural tolerance to homograft. In both cases, blocking antibody has an important role in the phenomenon of immunotolerance. From our experiments mentioned above transplantation and our earlier reported studies, we believe that the **hypo-antigenic fetal tissue** has distinct advantages over adult tissue for transplant purposes.

L21 ANSWER 5 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 2001643702 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11695808  
TITLE: A unique experience with human pre-immune (12 weeks) and hypo-immune (16 weeks) fetal thymus transplant in a vascular subcutaneous axillary fold in patients with advanced cancer: a report of two cases.  
AUTHOR: Bhattacharya N; Mukherjee K L; Chettri M K; Banerjee T; Bhattacharya S; Ghosh A; Bhattacharya M  
CORPORATE SOURCE: Principal Investigator of the Project and Surgeon Superintendent, Bijoygarh State Hospital, Calcutta, India.  
SOURCE: European journal of gynaecological oncology, (2001) 22 (4) 273-7.  
Journal code: 8100357. ISSN: 0392-2936.  
PUB. COUNTRY: Italy  
DOCUMENT TYPE: (CASE REPORTS)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200202  
ENTRY DATE: Entered STN: 20011107  
Last Updated on STN: 20020301  
Entered Medline: 20020228  
AB **BACKGROUND:** The **successful** development of fetal cell/tissue transplantation in adults has resulted in the possibility of eventual therapeutic solutions with a variety of intractable diseases. Umbilical cord whole blood transplantation appears to be safe in the adult system. In severe forms of DiGeorge Syndrome, cultured thymus transplant can help in the reconstitution of the immune condition of the host.  
**Successful fetal tissue** transplant in adults has raised the hope of future effective gene transplant and its manipulation prospects to combat many diseases including hemopathies, inborn errors of metabolism, immunodeficiencies and even cancer and AIDS.  
**MATERIALS AND METHOD:** Two cases of advanced cancer were treated with fetal (pre-immune 12 weeks and hypo-immune 16 weeks) thymus transplants in **subcutaneous** vascular axillary folds, which were **removed** after one month. Thymuses were collected from consenting mothers undergoing hysterotomy and ligation. **RESULTS AND ANALYSIS:** Patient 1 was suffering from non-Hodgkins lymphoma (Ann Arbor Stage IV) and was receiving cyclophosphamide, doxorubicin, vincristine and prednisolone after a course of radiotherapy; she developed leucopenia (2.400/cmm), which improved after receiving a 16-week human fetal thymic graft. The leucopenia was eventually over-corrected and the leucocyte count reached 44,000/cmm within a month, which was reversed after the thymus was taken out. Histology of the excised thymic graft showed growth and proliferation without any graft vs. host (GVH) reaction. Patient 2 was suffering from breast duct carcinoma (T4, N2, M0,) with estrogen, progesterone, and epidermal growth factor negative status, and was treated with modified radical mastectomy and axillary clearance followed by chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil for six cycles. She also received a 12-week-old human fetal thymus at the contra-lateral axilla which was **removed** after one month. In this case the peripheral leucocyte count did not show appreciable variation as in the first case. However, histology of the excised thymic graft showed growth and proliferation with an appearance of Hassel's corpuscles. **CONCLUSION:** Pre-immune and hypo-immune human fetal thymic transplant is not rejected in patients suffering from advanced cancer within one month (observation period). Thymic lymphocyte shedding in the



correction of leucopenia in the background of non-Hodgkin's lymphoma may have many therapeutic implications.

L21 ANSWER 6 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 1998382272 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9718146  
TITLE: Tissue repair in the fetal intestinal tract occurs with adhesions, fibrosis, and neovascularization.  
AUTHOR: Mast B A; Albanese C T; Kapadia S  
CORPORATE SOURCE: Division of Plastic and Reconstructive Surgery, University of Florida, Gainesville 32606, USA.  
SOURCE: Annals of plastic surgery, (1998 Aug) 41 (2) 140-4; discussion 144-7.  
Journal code: 7805336. ISSN: 0148-7043.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199810  
ENTRY DATE: Entered STN: 19981029  
Last Updated on STN: 19981029  
Entered Medline: 19981021

AB **Cutaneous** wound healing in the fetus can occur in a nonfibrotic, regenerative manner. However, other **fetal tissues** such as bone and stomach heal with scar formation. In light of potential ramifications for adult hollow visceral scarring (biliary and intestinal strictures), this study was undertaken to determine if tubular visceral tissue repair in the fetus is regenerative or fibrotic. Fetal rabbits underwent laparotomy on day 24 of gestation, during which a controlled intestinal enterotomy was created and suture repaired immediately using microsurgical techniques. Maternal rabbits and adult male rabbits also underwent enterotomy and repair. After 5 days all animals were sacrificed and the wounds analyzed histologically by a pathologist in a blinded fashion. All animals demonstrated a similar degree of peri-intestinal adhesion formation. Fetal and maternal wounds contained fibroblastic and smooth muscle cell proliferation, mild inflammatory infiltration, and new blood vessel formation. The male adult wounds demonstrated a more pronounced fibrovascular healing response. Immunohistochemical staining for CD31 (endothelial cell marker) was quantitated on a scale of 0 to 4+, indicating degree of neovascularization. The mean scores for the fetal and maternal groups were similar (1.70 +/- 0.68 and 1.23 +/- 1.07 respectively), but were significantly greater for male adults (2.93 +/- 0.12; p = 0.001 by analysis of variance). The results of this study indicate that hollow visceral tissue repair in the fetal rabbit intestine occurs in a similar fibrotic manner as adult healing. This provides further evidence that regenerative healing in the fetus is not ubiquitous. Differences in the degrees of fibrosis and neovascularization between adult male and pregnant female wounds deserve further investigation.

L21 ANSWER 7 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 96183561 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8618017  
TITLE: Detection of telomerase activity in malignant and nonmalignant skin conditions.  
AUTHOR: Taylor R S; Ramirez R D; Ogoshi M; Chaffins M; Piatyszek M A; Shay J W  
CORPORATE SOURCE: University of Texas Southwestern Medical Center at Dallas 75235, USA.  
CONTRACT NUMBER: AG07992 (NIA)  
SOURCE: Journal of investigative dermatology, (1996 Apr) 106 (4) 759-65.  
Journal code: 0426720. ISSN: 0022-202X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199606  
ENTRY DATE: Entered STN: 19960620  
Last Updated on STN: 19960620  
Entered Medline: 19960613

AB Telomeres are the end regions of linear chromosomes, and in normal somatic cells the lengths of telomeres shorten with **successive** cell divisions. Telomerase, a ribonucleoprotein enzyme, maintains the length of telomeres in immortal and germline cells. Although present in human **fetal tissues**, shortly after birth telomerase activity is not detectable except in germline cells, hematopoietic cells, and most human primary tumors. In the present study we show telomerase activity to be present in 73 of 77 basal cell carcinomas, 15 of 18 nonmetastatic **cutaneous** squamous cell carcinomas, and 6 of 7 **cutaneous** melanomas, contrasting with extremely low levels detected in sun-protected skin. Sun-damaged skin, psoriatic lesional skin, and skin from lesions of poison ivy dermatitis, however, have increased levels of telomerase activity compared to sun-protected skin, although less than that detected in tumor tissue. Because telomerase activity can be found in inflammatory lesions of the skin, this indicates that telomerase activity does not always correlate with the malignant phenotype. In addition, we show that telomerase activity is localized to the epidermis of newborn foreskin, which suggests that telomerase is expressed constitutively by cells in the epidermis. Finding higher levels of telomerase activity in sun-exposed skin compared to nonexposed skin suggests that environmental factors may modulate telomerase activity.

L21 ANSWER 8 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 94190591 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8142111  
TITLE: Evaluation of the teratogenic risk of cutaneously administered retinoids.  
AUTHOR: Buchan P  
CORPORATE SOURCE: CIRD Galderma, Sophia Antipolis, France.  
SOURCE: Skin pharmacology : official journal of the Skin Pharmacology Society, (1993) 6 Suppl 1 45-52. Ref: 22  
Journal code: 8810069. ISSN: 1011-0283.  
PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199405  
ENTRY DATE: Entered STN: 19940511  
Last Updated on STN: 19940511  
Entered Medline: 19940504

AB In current **cutaneous** retinoid therapy systemic exposure is low and the risk of teratogenesis appears to be limited. However, new indications, altered posologies and the introduction of new synthetic retinoids demand continuous assessment of the teratogenic risk. Teratogenicity testing of new substances in animals is only of value if accompanied by detailed pharmacokinetic analysis to establish the relationships between the levels of parent compound and metabolite in both maternal plasma and **fetal tissues** and teratogenic events. This information should be compared to the maximum of relevant pharmacokinetic data which can be ethically obtained in man or from human tissues. The presence or absence of teratogenic effects following **cutaneous** administration of retinoids in animals has, as **such**, little direct bearing on the risk in man. Two special cases exist where teratogenic risk can be evaluated directly in man without reference to animal studies. The first concerns substances whose teratogenic potential has been established in man by other routes of administration permitting a comparison with the **cutaneous** route on a pharmacokinetic basis. The second concerns the **cutaneous** administration of endogenously occurring substances and their eventual disturbance of systemic retinoid equilibrium.

L21 ANSWER 9 OF 13 MEDLINE on STN  
ACCESSION NUMBER: 92165012 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 1537521  
TITLE: Use of an animal model for the study of the role of human immunodeficiency virus 1 in the human intestine.  
COMMENT: Erratum in: Gastroenterology 1992 Sep;103(3):1123  
AUTHOR: Winter H S; Fox C H; Hendren R B; Isselbacher K J; Folkman J; Letvin N L

CORPORATE SOURCE: Department of Pediatrics, Children's Hospital, Boston, Massachusetts.  
CONTRACT NUMBER: AI27747 (NIAID)  
SOURCE: Gastroenterology, (1992 Mar) 102 (3) 834-9.  
Journal code: 0374630. ISSN: 0016-5085.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS  
ENTRY MONTH: 199204  
ENTRY DATE: Entered STN: 19920417  
Last Updated on STN: 19970203  
Entered Medline: 19920402

AB The gastrointestinal manifestations of human immunodeficiency virus (HIV)-1 disease have centered on identifiable causes of intestinal dysfunction **such** as parasitic and bacterial pathogens. The lamina propria of the intestine contains cell that harbor HIV-1, but the significance of this observation remains unknown. Because limited animal models are available to evaluate the gastrointestinal effects of this infection, a system that uses human fetal intestine transplanted **subcutaneously** onto the back of an immunodeficient mouse was developed. After 8 weeks, **fetal tissues** mature into an adult-appearing tissue with a lumen. Cell-free HIV-1 was inoculated into the explants, an evidence for infection was evaluated by histological evaluation, in situ hybridization, and polymerase chain reaction. No evidence for HIV-1 incorporation into epithelial cells could be found. It was concluded that this model provides a system in which intestinal HIV-1 interaction can be evaluated. In this model, cell-free HIV-1 does not appear to infect the epithelial cell.

L21 ANSWER 10 OF 13 MEDLINE on STN

ACCESSION NUMBER: 89192871 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 3240093  
TITLE: Cadmium and zinc concentrations in fetal and maternal rat tissue after parenteral administration of cadmium during pregnancy.  
AUTHOR: Roelfzema W H; Roelofsen A M; Herber R F; Peereboom-Steg J H  
CORPORATE SOURCE: Laboratory of Histology and Cell Biology, University of Amsterdam, The Netherlands.  
SOURCE: Archives of toxicology, (1988) 62 (4) 285-90.  
Journal code: 0417615. ISSN: 0340-5761.  
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198905  
ENTRY DATE: Entered STN: 19900306  
Last Updated on STN: 19970203  
Entered Medline: 19890505

AB Cadmium (Cd) and zinc (Zn) concentrations were determined by solid sampling atomic absorption spectrometry (AAS) in rat maternal and **fetal tissues** after exposure to cadmium. Cadmium was administered **subcutaneously** as CdCl<sub>2</sub> in saline daily during pregnancy. Two experiments were performed. In experiment I we investigated the tissue concentration at day 19 (gestational age) after administration of several doses: 0, 1.1, 2.2, 4.4, and 8.8  $\mu\text{mol Cd/kg/day}$ . In experiment II the course of the Cd and Zn concentrations during pregnancy was investigated by collecting samples at days 14, 16, 18 and 20, after daily injections of 4.4  $\mu\text{mol Cd/kg}$ . Cadmium concentrations in blood, maternal liver, placenta and fetal liver increased with dose and duration of exposure. Cadmium was heavily accumulated in the liver and transferred to the fetus only in small amounts. The zinc concentration in the maternal liver was positively correlated with the cadmium concentration. In the placenta the zinc concentration was not affected. Zinc in fetal liver was decreased from day 18 onward. Despite relatively high cadmium levels and decreased zinc levels in the fetus, we observed no adverse effects on various reproduction parameters, **such** as birth weights and obvious malformations.

L21 ANSWER 11 OF 13 MEDLINE on STN

ACCESSION NUMBER: 89080956 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 3204464  
 TITLE: Transforming growth factor beta (TGF-beta) induces fibrosis in a fetal wound model.  
 AUTHOR: Krummel T M; Michna B A; Thomas B L; Sporn M B; Nelson J M; Salzberg A M; Cohen I K; Diegelmann R F  
 CORPORATE SOURCE: Department of Surgery, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298-0015.  
 CONTRACT NUMBER: 20298  
 SOURCE: Journal of pediatric surgery, (1988 Jul) 23 (7) 647-52. Journal code: 0052631. ISSN: 0022-3468.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198902  
 ENTRY DATE: Entered STN: 19900308  
 Last Updated on STN: 19900308  
 Entered Medline: 19890209

AB The adult cellular response to tissue injury is characterized by acute inflammation followed eventually by fibroblast proliferation and collagen synthesis. Fetal tissue responses to injury differ markedly from those of the adult; an early acute inflammatory response is absent, few fibroblasts participate, and no collagen is deposited. The object of the present study was to analyze the effects of transforming growth factor beta (TGF-beta), an important regulatory molecule in adult healing events, on the fetal tissue response following wounding. Fetal cellular and extracellular matrix responses to injury were evaluated by placing subcutaneous wound implants containing TGF-beta (0.01 to 10 ng) in fetal rabbits at 24 days gestation (term = 31 days). Histologic responses one to seven days later were compared with fetal and adult control implants without TGF-beta. The histology of the adult implant was characterized by an early acute inflammatory response: by day 7 fibroblasts and collagen were predominant. In contrast, control implants removed from fetal rabbits had no histologic evidence of acute inflammation or fibroblast penetration and no collagen was deposited. When implants containing 1.0 ng TGF-beta were removed from fetal rabbits at seven days, a grossly fibrotic reaction was observed: histology confirmed marked fibroblast penetration with collagen deposition. Fetal implants containing 0.01 ng or 10 ng TGF-beta showed few fibroblasts but had increased numbers of inflammatory cells compared with controls. These observations demonstrate that the fetal response becomes adultlike with fibroblast proliferation and collagen accumulation when TGF-beta is added, thus documenting the responsiveness of the fetal system to adult repair signals. (ABSTRACT TRUNCATED AT 250 WORDS)

L21 ANSWER 12 OF 13 MEDLINE on STN  
 ACCESSION NUMBER: 87120767 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 3544283  
 TITLE: Passively acquired autoimmunity and the maternal fetal dyad in systemic lupus erythematosus.  
 AUTHOR: Buyon J; Szer I  
 SOURCE: Springer seminars in immunopathology, (1986) 9 (2-3) 283-304. Ref: 83  
 Journal code: 7910384. ISSN: 0344-4325.  
 PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198703  
 ENTRY DATE: Entered STN: 19900303  
 Last Updated on STN: 19900303  
 Entered Medline: 19870316

AB Neonatal lupus syndromes consist of transient cutaneous and hematologic abnormalities and permanent cardiac disorders all of which result from a common pathogenetic mechanism, the passive transfer of maternal autoantibodies. Detrimental antibodies such as SSA/Ro and SSB/La gain access to the fetal circulation via the normal active transport system of the trophoblast tissue which is operative after 20 weeks gestation. Despite functional maturation of the cardiac conduction

system by 16 weeks gestation, fetal bradycardias are most often encountered after this time. Several lines of evidence are advanced in this review to support the role of myocarditis as the initial consequence of autoantibody attack on the fetal heart. The end result of this inflammatory insult is permanent fibrosis manifest as complete congenital heart block (CCHB). Despite the clearly demonstrated presence of SSA/Ro and SSB/La in fetal tissues as well as their fluctuation in quantity during the cell cycle, the precise accessibility of these antigens to their respective autoantibodies is unknown at the present time. However, ultraviolet light is reported to induce cell surface expression of SSA/Ro on cultured keratinocytes. The recognition of CCHB by fetal echocardiogram is presented. The rationale for the use of dexamethasone which crosses the placenta in an active form to treat fetal immune effector functions is discussed. Intense maternal plasmapheresis in an attempt to rapidly decrease maternal autoantibodies may provide another approach to the management of CCHB. Through increasing knowledge of this model of "passively acquired pure" systemic lupus erythematosus, insights into mechanisms of tissue injury and strategies for treatment will emerge.

L21 ANSWER 13 OF 13 MEDLINE on STN  
 ACCESSION NUMBER: 77088419 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 831927  
 TITLE: Fetal complications of amniography.  
 AUTHOR: Grech P; Spitz L  
 SOURCE: British journal of radiology, (1977 Feb) 50 (590) 110-2.  
 Journal code: 0373125. ISSN: 0007-1285.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: (CASE REPORTS)  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 197703  
 ENTRY DATE: Entered STN: 19900313  
 Last Updated on STN: 19970203  
 Entered Medline: 19770331

AB In a series of 241 amniograms, there were two cases of **fetal tissue** damage resulting from the **subcutaneous** injection of contrast material. Details of these two cases are given and the damage sustained illustrated. Measures designed to prevent **such** complications are outlined, together with recommendations for its management, should **such** a complication occur.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
 L2 146532 S IN UTERO OR DONOR  
 L3 59250 S PERCUTAN?  
 L4 2 S L1 (S) L2 (S) 3  
 L5 0 S L1 (S) L2 (S) L3  
 L6 60 S L1 (S) L2  
 L7 23472 S INCISION  
 L8 0 S L1 (S) L2 (S) L7  
 L9 354581 S TRANSPLANT?  
 L10 14 S L1 (S) L2 (S) L9  
 L11 1197155 S SUCTION OR VACUUM OR SUC?  
 L12 1 S L1 (S) L2 (S) L9 (S) L11  
 L13 1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?  
 L14 1 S L1 (S) L2 (S) L9 (S) L13  
 L15 247721 S ?CUTAN?  
 L16 0 S L1 (S) L2 (S) L9 (S) L15  
 L17 0 S L1 (L) L2 (L) L9 (L) L15  
 L18 21 S L1 (L) L2 (L) L9 (L) L13  
 L19 64 S L1 (L) L15  
 L20 64 S L1 (L) L15 (L) L19  
 L21 13 S L1 (L) L15 (L) L19 (L) L13

=> s percutan?  
L22 59250 PERCUTAN?

=> s l1 (S) l22  
L23 0 L1 (S) L22

=> s l1 (1) l22  
L24 2 L1 (L) L22

=> d 1-2 ibib abs

L24 ANSWER 1 OF 2 MEDLINE on STN  
ACCESSION NUMBER: 1999387190 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10455432  
TITLE: Successful expression of beta-galactosidase and factor IX  
transgenes in fetal and neonatal sheep after  
ultrasound-guided percutaneous adenovirus vector  
administration into the umbilical vein.  
COMMENT: Comment in: Gene Ther. 1999 Jul;6(7):1200-1. PubMed ID:  
10455427  
AUTHOR: Themis M; Schneider H; Kiserud T; Cook T; Adebakin S;  
Jezzard S; Forbes S; Hanson M; Pavirani A; Rodeck C;  
Coutelle C  
CORPORATE SOURCE: Cystic Fibrosis Gene Therapy Research Group, Section of  
Molecular Genetics, Division of Biomedical Sciences,  
Imperial College School of Medicine, London, UK.  
SOURCE: Gene therapy, (1999 Jul) 6 (7) 1239-48.  
Journal code: 9421525. ISSN: 0969-7128.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200002  
ENTRY DATE: Entered STN: 20000309  
Last Updated on STN: 20000320  
Entered Medline: 20000224

AB In utero somatic gene therapy in the later stages of pregnancy may allow  
targeting of organ systems which are difficult to reach later in life and  
to prevent the development of tissue damage otherwise caused by the early  
onset of inherited diseases. We report here on the **percutaneous**  
delivery of two adenoviral vectors, containing the beta-galactosidase  
reporter gene and the human Factor IX gene respectively, to the fetal  
liver and circulation by ultrasound-guided umbilical vein puncture similar  
to procedures used in human pregnancy. Vector spread, as detected by PCR  
analysis for the beta-galactosidase encoding vector, was found in almost  
all fetal and neonatal organs and in the maternal liver. Expression of  
the beta-galactosidase transgene was detected in many **fetal**  
**tissues** by RT-PCR. High beta-galactosidase production was shown  
by immuno-histochemistry predominantly in the liver, where about 30percent  
of the hepatocytes stained positive, and in the adrenal cortex.  
Production of factor IX was determined by ELISA in the plasma of treated  
fetuses and newborn lambs and reached at birth up to 80percent of the  
normal human plasma concentration. This demonstrates a very hopeful proof  
of principle for the development of prenatal treatment of many genetic  
diseases but also requires more detailed investigations with respect to  
the observed systemic spread of the vector.

L24 ANSWER 2 OF 2 MEDLINE on STN  
ACCESSION NUMBER: 91051741 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2240113  
TITLE: Direct analysis of uncultured cytotrophoblastic cells from  
second- and third-trimester placentas: an accurate and  
rapid method for detection of fetal chromosome  
abnormalities.  
AUTHOR: Shulman L P; Tharapel A T; Meyers C M; Phillips O P;  
Simpson J L; Elias S  
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of  
Tennessee, Memphis 38163.  
CONTRACT NUMBER: HD-22968 (NICHD)  
HD-82904 (NICHD)  
SOURCE: American journal of obstetrics and gynecology, (1990 Nov)

163 (5 Pt 1) 1606-9.  
 Journal code: 0370476. ISSN: 0002-9378.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199012  
 ENTRY DATE: Entered STN: 19910208  
 Last Updated on STN: 20020125  
 Entered Medline: 19901214

AB Transabdominal chorionic villus sampling can be readily used for detection of fetal chromosome abnormalities in the second and third trimesters of pregnancy. Although culture of chorionic villi offers little advantage over cultured amniotic fluid cells with respect to time required to obtain results, cytogenetic analysis of chorionic villi by direct analysis of uncultured cytotrophoblastic cells offers clear advantages because of the very short time required to obtain results. To determine whether direct analysis of uncultured cytotrophoblastic cells from second- and third-trimester placentas can routinely provide rapid and accurate assessment of fetal status, we evaluated chorionic villus specimens obtained from 57 placentas; 49 placentas were sampled in the second trimester whereas eight were sampled in the third trimester. Direct preparations yielded karyotypes in 56 (98.2%) preparations; all results of direct analyses were available within 72 hours and, when requested, within 12 hours. All results were confirmed by chromosome analysis of cultured mesenchymal core cells or cultured fetal tissue. We conclude that direct analysis of cytotrophoblastic cells from second- and third-trimester placentas is a very rapid and accurate method for determining fetal chromosome status that is comparable with, if not superior to, percutaneous umbilical blood sampling.

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(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
 L2 146532 S IN UTERO OR DONOR  
 L3 59250 S PERCUTAN?  
 L4 2 S L1 (S) L2 (S) 3  
 L5 0 S L1 (S) L2 (S) L3  
 L6 60 S L1 (S) L2  
 L7 23472 S INCISION  
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 L15 247721 S ?CUTAN?  
 L16 0 S L1 (S) L2 (S) L9 (S) L15  
 L17 0 S L1 (L) L2 (L) L9 (L) L15  
 L18 21 S L1 (L) L2 (L) L9 (L) L13  
 L19 64 S L1 (L) L15  
 L20 64 S L1 (L) L15 (L) L19  
 L21 13 S L1 (L) L15 (L) L19 (L) L13  
 L22 59250 S PERCUTAN?  
 L23 0 S L1 (S) L22  
 L24 2 S L1 (L) L22

=> s 12 (S) 122

L25 79 L2 (S) L22

=> s fetal

215418 FETAL

6 FETALS

L26 215420 FETAL

(FETAL OR FETALS)

=> s 12 (S) 122 (S) 126  
L27 8 L2 (S) L22 (S) L26

=> d 1-2 ibib abs

L27 ANSWER 1 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 2003599387 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14681699  
TITLE: Widespread and efficient marker gene expression in the  
airway epithelia of fetal sheep after minimally invasive  
tracheal application of recombinant adenovirus in utero.  
AUTHOR: Peebles D; Gregory L G; David A; Themis M; Waddington S N;  
Knapton H J; Miah M; Cook T; Lawrence L; Nivsarkar M;  
Rodeck C; Coutelle C  
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Royal Free and  
University College Medical School, London, UK.  
SOURCE: Gene therapy, (2004 Jan) 11 (1) 70-8.  
Journal code: 9421525. ISSN: 0969-7128.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200404  
ENTRY DATE: Entered STN: 20031219  
Last Updated on STN: 20040423  
Entered Medline: 20040422

AB Cystic fibrosis is a common lethal genetic disease caused by functional  
absence of the cystic fibrosis transmembrane conductance regulator (CFTR).  
Although a candidate disease for in utero gene therapy, demonstration of  
potentially therapeutic levels of transgene expression in the fetal  
airways after minimally invasive gene delivery is a mandatory prerequisite  
before application of this approach in humans can be considered. We  
report here on the delivery of a beta-galactosidase expressing adenovirus  
directly to the airways of fetal sheep in utero using  
ultrasound-guided percutaneous injection of the trachea in the  
fetal chest. Injection of adenoviral particles to the fetal  
airways was not associated with mortality and resulted in low-level  
expression in the peripheral airways. However, complexation of the virus  
with DEAE dextran, which confers a positive charge to the virus, and  
pretreatment of the airways with Na-caprate, which opens tight junctions,  
increased transgene expression, and a combination of these two enhancers  
resulted in widespread and efficient gene transfer of the fetal trachea  
and bronchial tree. Using a percutaneous ultrasound-guided injection  
technique, we have clearly demonstrated proof of principle for substantial  
transgene delivery to the fetal airways providing levels of gene  
expression that could be relevant for a therapeutic application of CFTR  
expressing vectors.

L27 ANSWER 2 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 2003144731 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12659676  
TITLE: Ultrasound-guided percutaneous delivery of  
adenoviral vectors encoding the beta-galactosidase and  
human factor IX genes to early gestation fetal  
sheep in utero.  
AUTHOR: David Anna; Cook Terry; Waddington Simon; Peebles Donald;  
Nivsarkar Megha; Knapton Holly; Miah Maznu; Dahse Thomas;  
Noakes David; Schneider Holm; Rodeck Charles; Coutelle  
Charles; Themis Mike  
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Royal Free and  
University College Medical School, 86-96 Chenies Mews,  
London, WC1E 6HX, United Kingdom.. a.david@ucl.ac.uk  
SOURCE: Human gene therapy, (2003 Mar 1) 14 (4) 353-64.  
Journal code: 9008950. ISSN: 1043-0342.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200309  
ENTRY DATE: Entered STN: 20030328  
Last Updated on STN: 20030928



Entered Medline: 20030926

AB In utero gene therapy may provide treatment of genetic diseases before significant organ damage, allow permanent genetic correction by reaching stem cell populations, and provide immune tolerance against the therapeutic transgenes and vectors. We have used percutaneous ultrasound-guided injection as a minimally invasive fetal procedure. First-generation adenoviruses encoding the nuclear localizing beta-galactosidase reporter gene or the human factor IX (hFIX) gene, or colloidal carbon were delivered via the umbilical vein (UV, n = 4), heart (intracardiac [IC], n = 2), liver parenchyma (intrahepatic [HE], n = 11), peritoneal cavity (intraperitoneal [IP], n = 14), skeletal musculature ([intramuscular [IM], n = 11), or the amniotic cavity (intraamniotic [IA], n = 14) to early-gestation fetal sheep (0.3 gestation = day 33-61). Postmortem analysis was performed at 2, 9, or 28 days after injection. Although fetal survival was between 77% and 91% for IP, HE, IA, and IM routes, no fetuses survived UV or IC procedures. The hFIX levels reaching 1900 and 401 ng/ml (IP), 30 ng/ml (HE), 66.5 and 39 ng/ml (IA), and 83 and 65.5 ng/ml (IM), respectively, were determined 2 days after injection and decreased at birth to 16.5 ng/ml (IP), 7 ng/ml (HE), 4.5 ng/ml (IA), and 4 and 0 ng/ml (IM). Polymerase chain reaction (PCR) and immunohistochemistry showed broadest hFIX transgene spread and highest localised beta-galactosidase expression, respectively, after IP administration. Antibodies were observed against vector but not against hFIX.

=> d 1-8 ibib abs

L27 ANSWER 1 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 2003599387 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14681699  
TITLE: Widespread and efficient marker gene expression in the airway epithelia of fetal sheep after minimally invasive tracheal application of recombinant adenovirus in utero.  
AUTHOR: Peebles D; Gregory L G; David A; Themis M; Waddington S N; Knapton H J; Miah M; Cook T; Lawrence L; Nivsarkar M; Rodeck C; Coutelle C  
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Royal Free and University College Medical School, London, UK.  
SOURCE: Gene therapy, (2004 Jan) 11 (1) 70-8.  
JOURNAL code: 9421525. ISSN: 0969-7128.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200404  
ENTRY DATE: Entered STN: 20031219  
Last Updated on STN: 20040423  
Entered Medline: 20040422

AB Cystic fibrosis is a common lethal genetic disease caused by functional absence of the cystic fibrosis transmembrane conductance regulator (CFTR). Although a candidate disease for in utero gene therapy, demonstration of potentially therapeutic levels of transgene expression in the fetal airways after minimally invasive gene delivery is a mandatory prerequisite before application of this approach in humans can be considered. We report here on the delivery of a beta-galactosidase expressing adenovirus directly to the airways of fetal sheep in utero using ultrasound-guided percutaneous injection of the trachea in the fetal chest. Injection of adenoviral particles to the fetal airways was not associated with mortality and resulted in low-level expression in the peripheral airways. However, complexation of the virus with DEAE dextran, which confers a positive charge to the virus, and pretreatment of the airways with Na-caprate, which opens tight junctions, increased transgene expression, and a combination of these two enhancers resulted in widespread and efficient gene transfer of the fetal trachea and bronchial tree. Using a percutaneous ultrasound-guided injection technique, we have clearly demonstrated proof of principle for substantial transgene delivery to the fetal airways providing levels of gene expression that could be relevant for a therapeutic application of CFTR expressing vectors.

L27 ANSWER 2 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2003144731 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 12659676  
 TITLE: Ultrasound-guided **percutaneous** delivery of adenoviral vectors encoding the beta-galactosidase and human factor IX genes to early gestation **fetal** sheep in **utero**.  
 AUTHOR: David Anna; Cook Terry; Waddington Simon; Peebles Donald; Nivsarkar Megha; Knapton Holly; Miah Maznu; Dahse Thomas; Noakes David; Schneider Holm; Rodeck Charles; Coutelle Charles; Themis Mike  
 CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Royal Free and University College Medical School, 86-96 Chenies Mews, London, WC1E 6HX, United Kingdom.. a.david@ucl.ac.uk  
 SOURCE: Human gene therapy, (2003 Mar 1) 14 (4) 353-64.  
 Journal code: 9008950. ISSN: 1043-0342.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200309  
 ENTRY DATE: Entered STN: 20030328  
 Last Updated on STN: 20030928  
 Entered Medline: 20030926  
 AB In utero gene therapy may provide treatment of genetic diseases before significant organ damage, allow permanent genetic correction by reaching stem cell populations, and provide immune tolerance against the therapeutic transgenes and vectors. We have used percutaneous ultrasound-guided injection as a minimally invasive fetal procedure. First-generation adenoviruses encoding the nuclear localizing beta-galactosidase reporter gene or the human factor IX (hFIX) gene, or colloidal carbon were delivered via the umbilical vein (UV, n = 4), heart (intracardiac [IC], n = 2), liver parenchyma (intrahepatic [HE], n = 11), peritoneal cavity (intraperitoneal [IP], n = 14), skeletal musculature ([intramuscular [IM], n = 11), or the amniotic cavity (intraamniotic [IA], n = 14) to early-gestation fetal sheep (0.3 gestation = day 33-61). Postmortem analysis was performed at 2, 9, or 28 days after injection. Although fetal survival was between 77% and 91% for IP, HE, IA, and IM routes, no fetuses survived UV or IC procedures. The hFIX levels reaching 1900 and 401 ng/ml (IP), 30 ng/ml (HE), 66.5 and 39 ng/ml (IA), and 83 and 65.5 ng/ml (IM), respectively, were determined 2 days after injection and decreased at birth to 16.5 ng/ml (IP), 7 ng/ml (HE), 4.5 ng/ml (IA), and 4 and 0 ng/ml (IM). Polymerase chain reaction (PCR) and immunohistochemistry showed broadest hFIX transgene spread and highest localised beta-galactosidase expression, respectively, after IP administration. Antibodies were observed against vector but not against hFIX.

L27 ANSWER 3 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2002251214 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11991414  
 TITLE: Percutaneous collection of fetal fluids for detection of bovine viral diarrhea virus infection in cattle.  
 AUTHOR: Callan Robert J; Schnackel John A; Van Campen Hana; Mortimer Robert G; Cavender Jacqueline A; Williams Elizabeth S  
 CORPORATE SOURCE: Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins 80523-1620, USA.  
 SOURCE: Journal of the American Veterinary Medical Association, (2002 May 1) 220 (9) 1348-52.  
 Journal code: 7503067. ISSN: 0003-1488.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200207  
 ENTRY DATE: Entered STN: 20020507  
 Last Updated on STN: 20020731  
 Entered Medline: 20020730  
 AB OBJECTIVE: To develop a method for percutaneous collection of fetal fluid

from cattle in the late stages of gestation and determine whether bovine viral diarrhoea virus (BVDV) can be isolated from such fluids. DESIGN: Case series. ANIMALS: 169 pregnant beef cattle. PROCEDURE: Animals were restrained in a squeeze chute, and hair was clipped from a region of the right flank. Pregnancy was confirmed, and fetal fluids were identified by means of abdominal ultrasonography. Fetal fluid was collected with a spinal needle. Virus isolation was performed on fetal fluids, WBC lysates from 160 live calves, and tissues from 12 calves that died or were aborted. Blood samples collected from adult cattle were assayed with an immunoperoxidase monolayer assay. RESULTS: Fourteen animals aborted or delivered premature calves within 3 weeks after fetal fluid collection; however, it could not be determined whether this was a complication of the procedure or attributable to other factors. Results of BVDV isolation from fetal fluid samples were negative for 168 animals. However, a noncytopathic BVDV was isolated from fetal fluid obtained from a 2-year-old heifer; results of the immunoperoxidase assay of serum from this heifer were also positive, and a noncytopathic BVDV was isolated from tissue specimens from a stillborn calf produced by this heifer. CONCLUSIONS AND CLINICAL RELEVANCE: Results suggest that fetal fluids can be collected **percutaneously** from cattle in the late stages of gestation and that virus isolation performed on fetal fluids can be used to identify fetuses infected with BVDV in **utero**. However, safety of the procedure could not be evaluated.

L27 ANSWER 4 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 95387727 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 7658779  
 TITLE: In-utero **percutaneous** cystoscopy in the management of fetal lower obstructive uropathy.  
 AUTHOR: Quintero R A; Johnson M P; Romero R; Smith C; Arias F; Guevara-Zuloaga F; Cotton D B; Evans M I  
 CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Hutzel Hospital/Wayne State University, Detroit, MI, USA.  
 SOURCE: Lancet, (1995 Aug 26) 346 (8974) 537-40.  
 Journal code: 2985213R. ISSN: 0140-6736.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
 ENTRY MONTH: 199510  
 ENTRY DATE: Entered STN: 19951013  
 Last Updated on STN: 20000303  
 Entered Medline: 19951003

AB In fetuses with lower obstructive uropathy, sonography cannot establish the cause of obstruction. We assessed whether **percutaneous fetal** cystoscopy could be useful in the evaluation and treatment of obstructive defects in **utero**. We inserted a fiberoptic endoscope through the lumen of the needle or trocar into the fetal bladder at the time of vesicocentesis or vesicoamniotic-shunt placement and looked at the urethra, bladder neck, and ureteral orifices. Urethral vesicoamniotic shunting was considered in suitable cases; otherwise a percutaneous shunt was inserted. Fetal cystoscopy was possible in 11 of 13 patients referred. The bladder mucosa appeared haemorrhagic or oedematous in three. The ureteral orifices were seen in 9/11 fetuses, dilation was seen in five, but was only suspected in two by ultrasound. Ureteral webs were noted in two other fetuses. Two of seven fetuses underwent urethral vesicoamniotic shunting; urethral patency was achieved with urethral probing alone in one fetus. The remaining four fetuses were shunted with a standard technique. Fetal cystoscopy helps define the underlying conditions responsible for sonographic findings of lower obstructive uropathy, and allows the introduction of new treatments.

L27 ANSWER 5 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 95245463 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 7728265  
 TITLE: [Platelet transfusions in neonatology].  
 Transfusions plaquettaires en neonatalogie.  
 AUTHOR: Chabernaud J L; Lacaze T; Zupan V; Boithias C; Gross E; Dehan M  
 CORPORATE SOURCE: Service de reanimation neonatale, Hopital Antoine-Beclere, Clamart.

SOURCE: Transfusion clinique et biologique : journal de la Societe  
francaise de transfusion sanguine, (1995) 2 (1) 17-25.  
Ref: 27  
Journal code: 9423846. ISSN: 1246-7820.

PUB. COUNTRY: France

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: French

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199505

ENTRY DATE: Entered STN: 19950608  
Last Updated on STN: 19960129  
Entered Medline: 19950530

AB Thrombocytopenia occurs in 20% to 40% of infants admitted to a neonatal intensive care unit. Approximately 30% of the newborns with severe thrombocytopenia below 50.10(9)/l platelets receive platelet transfusions. The etiology may be: bacterial infection, DIC and immune mediated thrombocytopenia. The consequences of thrombocytopenia are significant risks of severe intracranial hemorrhage and neurologic morbidity. Therapeutic platelet transfusions are given to actively bleeding neonates with less than 50.10(9)/l platelets. Prophylactic platelet concentrates are usually given to infants with platelets counts below 20.10(9)/l. The standard platelet concentrate (CMV-negative donor) is the product of choice for newborns. Fetal intracranial hemorrhage is possible as soon as 20 weeks of gestation in allo-immune thrombocytopenia. Actually **percutaneous** umbilical blood sampling is very useful to measure **fetal** platelets count in order to decide in **utero** maternal platelet transfusion. Maternal irradiated plateletpheresis concentrates are preferentially infused in this indication. At the end of pregnancy, cesarean section is preferred to normal vaginal delivery if fetal thrombocytopenia below 100.10(9)/l is observed. In pregnant women with auto-immune thrombocytopenia, the decision to carry out percutaneous umbilical blood samples should be weigh relatively to the 3-5% estimated risk of serious consequences. Platelets transfusions are particularly successful in immune thrombocytopenia but less effective in other clinical circumstances.

L27 ANSWER 6 OF 8 MEDLINE on STN

ACCESSION NUMBER: 94340320 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8062030

TITLE: Fetal obstructive uropathy.

AUTHOR: Estes J M; Harrison M R

CORPORATE SOURCE: Department of Surgery, New England Deaconess Hospital,  
Boston, MA.

SOURCE: Seminars in pediatric surgery, (1993 May) 2 (2) 129-35.  
Ref: 31  
Journal code: 9216162. ISSN: 1055-8586.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199409

ENTRY DATE: Entered STN: 19941005  
Last Updated on STN: 19941005  
Entered Medline: 19940920

AB Congenital obstructive uropathy is a relatively common developmental malformation, and severely affected fetuses die soon after birth from oligohydramnios-induced pulmonary hypoplasia or renal failure. Prenatal ultrasonography can reliably diagnose the specific anatomic defect, and using fetal urine sampling we can determine the extent of renal damage in utero with reasonable certainty. With these diagnostic tools and an understanding of the natural history of congenital obstructive uropathy we can now make rational decisions regarding treatment. Clinical experience has demonstrated that the selected fetus may benefit from in **utero** decompression, either by **percutaneous** shunt placement or open **fetal** surgery. However, each of these procedures has certain risks that must be carefully weighed against the expected benefits. Future techniques using fetoscopic surgery may provide the ideal

therapeutic approach.

L27 ANSWER 7 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 90166918 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2696540  
TITLE: Common fetal urinary tract anomalies.  
AUTHOR: Manning F A  
SOURCE: Clinics in diagnostic ultrasound, (1989) 25 139-61. Ref:  
40  
Journal code: 7904770. ISSN: 0193-743X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199004  
ENTRY DATE: Entered STN: 19900601  
Last Updated on STN: 19900601  
Entered Medline: 19900412

AB The role of ultrasound in detecting fetal anomalies in general and genitourinary tract anomalies in particular has undergone, and continues to undergo, remarkable changes. The diagnostic process began with a focus on the structural nature of anomalies and now has moved forward to include a detailed assessment of the functional nature and sequelae of these lesions. Concurrent with this shift in diagnostic emphasis has been the development of the role of ultrasonography in guiding invasive diagnostic procedures, such as percutaneous fetal blood sampling and fetal urine aspiration, and in guiding therapeutic procedures, such as chronic in utero vesicoamniotic shunt placement. These changes are occurring against a background of the role of ultrasound in assessing pathophysiology of the anomaly and assignment of prognosis, two decisions that profoundly influence pregnancy management. The challenge for the perinatal ultrasonographer is now not only to recognize the lesion, but also to institute the further investigative steps upon which a rational management plan may be based. As illustrated in this brief review of the more common genitourinary tract anomalies, the range of outcome and the pathophysiologic progression of the disease are both wide and complex. Continued improvements in ultrasound technologies and application hold the key to the ultimate reduction in the clinical significance of these common fetal diseases.

L27 ANSWER 8 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 89323501 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2752169  
TITLE: Perinatal diagnosis of passive ITP: use of percutaneous umbilical blood sampling (PUBS).  
AUTHOR: Sacher R A; King J C  
CORPORATE SOURCE: Department of Laboratory Medicine, Georgetown University Medical Center, Washington.  
SOURCE: Blut, (1989 Jul) 59 (1) 128-31.  
Journal code: 0173401. ISSN: 0006-5242.  
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198908  
ENTRY DATE: Entered STN: 19900309  
Last Updated on STN: 19900309  
Entered Medline: 19890829

AB Fetal blood samples can be obtained in utero by direct sampling of the umbilical cord vessels, using an ultrasound guided technique termed percutaneous umbilical sampling (PUBS). This procedure is being used more frequently in high risk pregnancies to obtain direct fetal laboratory data. In specialized centers, with trained personnel, the technique can be used with a high degree of safety and efficiency. Direct access to the fetal circulation can also allow an accurate determination of the fetal platelet count in cases of suspected fetal thrombocytopenia. The technique may be used to plan appropriate clinical management of maternal ITP as well as to diagnose the presence of fetal alloimmune thrombocytopenia. A logical strategy for obstetric

management and evaluation of fetal risk can be planned. The procedure also has the potential to allow direct fetal treatment as has been the case in the management of severe fetal anemia.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

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L1      6659 S FETAL TISSUE
L2      146532 S IN UTERO OR DONOR
L3      59250 S PERCUTAN?
L4      2 S L1 (S) L2 (S) 3
L5      0 S L1 (S) L2 (S) L3
L6      60 S L1 (S) L2
L7      23472 S INCISION
L8      0 S L1 (S) L2 (S) L7
L9      354581 S TRANSPLANT?
L10     14 S L1 (S) L2 (S) L9
L11     1197155 S SUCTION OR VACUUM OR SUC?
L12     1 S L1 (S) L2 (S) L9 (S) L11
L13     1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?
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L18     21 S L1 (L) L2 (L) L9 (L) L13
L19     64 S L1 (L) L15
L20     64 S L1 (L) L15 (L) L19
L21     13 S L1 (L) L15 (L) L19 (L) L13
L22     59250 S PERCUTAN?
L23     0 S L1 (S) L22
L24     2 S L1 (L) L22
L25     79 S L2 (S) L22
L26     215420 S FETAL
L27     8 S L2 (S) L22 (S) L26
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=> file biosis embase caplus pctful uspatful scisearch medline confsci		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	28.09	28.30

FILE 'BIOSIS' ENTERED AT 15:57:23 ON 20 JUL 2004  
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FILE 'USPATFULL' ENTERED AT 15:57:23 ON 20 JUL 2004  
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE 'MEDLINE' ENTERED AT 15:57:23 ON 20 JUL 2004

FILE 'CONFSCI' ENTERED AT 15:57:23 ON 20 JUL 2004  
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4 FILES SEARCHED...  
L28 80 L14

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ENTER L# LIST OR (END):128
PROCESSING COMPLETED FOR L28
L29      69 DUP REM L28 (11 DUPLICATES REMOVED)
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=> s 116
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LEFT TRUNCATION IGNORED FOR '?CUTAN?' FOR FILE 'CONFSCI'
L30      5 L16
Left truncation is not valid in the specified search field in the
specified file. The term has been searched without left truncation.
Examples: '?TERPEN?' would be searched as 'TERPEN?' and '?FLAVONOID'
would be searched as 'FLAVONOID.'
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If you are searching in a field that uses implied proximity, and you used a truncation symbol after a punctuation mark, the system may interpret the truncation symbol as being at the beginning of a term. Implied proximity is used in search fields indexed as single words, for example, the Basic Index.

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=> d 1-5 ibib abs
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L30      ANSWER 1 OF 5      PCTFULL  COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER:      2001062891 PCTFULL  ED 20020822
TITLE (ENGLISH):      207 HUMAN SECRETED PROTEINS
TITLE (FRENCH):      207 PROTEINES HUMAINES SECRETEES
INVENTOR(S):      NI, Jian;
                  EBNER, Reinhard;
                  LAFLEUR, David, W.;
                  MOORE, Paul, A.;
                  OLSEN, Henrik, S.;
                  ROSEN, Craig, A.;
                  RUBEN, Steven, M.;
                  SOPPET, Daniel, R.;
                  YOUNG, Paul, E.;
                  SHI, Yanggu;
                  FLORENCE, Kimberly, A.;
                  WEI, Ying-Fei;
                  FLORENCE, Charles;
                  HU, Jing-Shan;
                  LI, Yi;
                  KYAW, Hla;
                  FISCHER, Carrie, L.;
                  FERRIE, Ann, M.;
                  FAN, Ping;
                  FENG, Ping;
                  ENDRESS, Gregory, A.;
                  DILLON, Patrick, J.;
                  CARTER, Kennith, C.;
                  BREWER, Laurie, A.;
                  YU, Guo-Liang;
                  ZENG, Zhizhen;
                  GREENE, John, M.
PATENT ASSIGNEE(S):      HUMAN GENOME SCIENCES, INC.;
                  NI, Jian;
                  EBNER, Reinhard;
                  LAFLEUR, David, W.;
                  MOORE, Paul, A.;
                  OLSEN, Henrik, S.;
                  ROSEN, Craig, A.;
                  RUBEN, Steven, M.;
                  SOPPET, Daniel, R.;
                  YOUNG, Paul, E.;
                  SHI, Yanggu;
                  FLORENCE, Kimberly, A.;
                  WEI, Ying-Fei;
                  FLORENCE, Charles;
                  HU, Jing-Shan;
                  LI, Yi;
                  KYAW, Hla;
```

FISCHER, Carrie, L.;  
FERRIE, Ann, M.;  
FAN, Ping;  
FENG, Ping;  
ENDRESS, Gregory, A.;  
DILLON, Patrick, J.;  
CARTER, Kennith, C.;  
BREWER, Laurie, A.;  
YU, Guo-Liang;  
ZENG, Zhizhen;  
GREENE, John, M.  
Patent

DOCUMENT TYPE:  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001062891	A2	20010830

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US5614 A 20010221  
PRIORITY INFO.: US 2000-60/184,836 20000224  
US 2000-60/193,170 20000329

ABEN The present invention relates to the novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

ABFR La presente invention concerne de nouvelles proteines humaines secretees ainsi que des acides nucleiques isoles contenant les regions codantes des genes codant ces proteines. L'invention concerne egalement des vecteurs, des cellules hotes, des anticorps ainsi que des methodes de recombinaison permettant la production de proteines humaines secretees. L'invention concerne egalement des methodes de diagnostic et therapeutiques utiles pour diagnostiquer et traiter des maladies, des troubles et/ou des etats lies a ces nouvelles proteines humaines secretees.

L30 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2001042451 PCTFULL ED 20020827  
TITLE (ENGLISH): FULL-LENGTH HUMAN cDNAs ENCODING POTENTIALLY SECRETED PROTEINS  
TITLE (FRENCH): ADNc HUMAINS PLEINE LONGUEUR CODANT POUR DES PROTEINES POTENTIELLEMENT SECRETEES  
INVENTOR(S): DUMAS MILNE EDWARDS, Jean-Baptiste;  
BOUGUELERET, Lydie;  
JOBERT, Severin  
PATENT ASSIGNEE(S): GENSET;  
DUMAS MILNE EDWARDS, Jean-Baptiste;  
BOUGUELERET, Lydie;  
JOBERT, Severin  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001042451	A2	20010614

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF



CG CI CM GA GN GW ML MR NE SN TD TG  
 APPLICATION INFO.: WO 2000-IB1938 A 20001207  
 PRIORITY INFO.: US 1999-60/169,629 19991208  
 US 2000-60/187,470 20000306

ABEN The invention concerns GENSET polynucleotides and polypeptides. Such GENSET products may be used as reagents in forensic analyses, as chromosome markers, as tissue/cell/organelle-specific markers, in the production of expression vectors. In addition, they may be used in screening and diagnosis assays for abnormal GENSET expression and/or biological activity and for screening compounds that may be used in the treatment of GENSET-related disorders.

ABFR L'invention concerne des polynucleotides et des polypeptides GENSET. Ces produits GENSET peuvent s'utiliser comme reactifs dans des analyses judiciaires, en tant que marqueurs chromosomiques, comme marqueurs specifiques a un tissu/cellule/organite, dans la production de vecteurs d'expression. En outre, ils peuvent s'utiliser dans des dosages de criblage et diagnostiques d'une expression GENSET et/ou une activite biologique anormales ainsi que pour le criblage de composes pouvant etre utilises dans le traitement de troubles lies a GENSET.

L30 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 1995009235 PCTFULL ED 20020514  
 TITLE (ENGLISH): IMMUNODEFICIENT MOUSE MODELS OF PATHOGENESIS OF HUMAN DISEASE AND EFFICACY AND TOXICITY OF DISEASE TREATMENTS  
 TITLE (FRENCH): MODELES DE SOURIS IMMUNODEFICIENTES POUR ANALYSER LA PATHOGENESE DE MALADIES HUMAINES ET L'EFFICACITE ET LA TOXICITE DES TRAITEMENTS UTILISES  
 INVENTOR(S): GOLDSTEIN, Harris;  
 KOLLMANN, Tobias, R.  
 PATENT ASSIGNEE(S): ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9509235	A1	19950406

# DESIGNATED STATES

W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE  
 APPLICATION INFO.: WO 1994-US10957 A 19940928  
 PRIORITY INFO.: US 1993-127,880 19930928  
 US 1994-252,773 19940602

ABEN BTCD-hu2 chimeric mice for assaying the pathogenesis of human disease and efficacy and toxicity of disease treatments have been developed by implantation of human fetal thymus and human fetal liver tissue under the kidney capsule of T- and B-cell deficient mice, by engraftment of human fetal bone marrow cells into T- and B-cell deficient mice and combinations of both. The resulting chimeric mice contain human T-cells, human monocytes or combinations thereof in sufficient quantity in the mouse peripheral lymphoid compartment to support HIV-1 infection following intraperitoneal inoculation of HIV-1 into the mouse.

ABFR Souris chimeriques BTCD-hu2 destinees a l'etude de la pathogenese de maladies humaines et a evaluer l'efficacite et la toxicite des traitements utilises, produites par implantation de tissus de foie et de thymus de foetus humains sous la capsule du rein de souris presentant une deficiencie en lymphocytes T et B, par greffe de cellules de moelle osseuse foetale humaine sur des souris presentant une deficiencie en lymphocytes T et B et des combinaisons des deux. Les souris chimeriques qui en resultent contiennent dans leur compartiment lymphoide peripherique des lymphocytes T humains, des monocytes humains ou des combinaisons des deux en quantite suffisante pour supporter une infection par le VIH-1 a la suite de l'inoculation intraperitoneale de VIH-1 chez lesdites

souris.

L30 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1995005843 PCTFULL ED 20020514  
TITLE (ENGLISH): METHOD FOR PRODUCING A HIGHLY ENRICHED POPULATION OF  
HEMATOPOIETIC STEM CELLS  
TITLE (FRENCH): PROCEDE DE PRODUCTION D'UNE POPULATION DE CELLULES  
SOUCHES HEMATOPOIETIQUES FORTEMENT ENRICHIE  
INVENTOR(S): DiGIUSTO, David;  
GALY, Anne  
PATENT ASSIGNEE(S): SYSTEMIX, INC.;  
DiGIUSTO, David;  
GALY, Anne  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505843	A1	19950302

DESIGNATED STATES  
W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL  
PT SE  
APPLICATION INFO.: WO 1994-US9760 A 19940825  
PRIORITY INFO.: US 1993-8/112,603 19930825  
ABEN The present invention provides a simple and reliable means for isolating  
populations of  
hematopoietic cells enriched for stem cell activity on the basis of  
possession of high CD34 cell  
surface antigen density (CD34hi). CD34hi cell preparations are useful,  
for example, for drug  
discovery efforts, for reconstituting hematopoiesis in an animal lacking  
a functioning hematopoietic  
system, and for gene therapies.  
ABFR L'invention constitue un moyen simple et de grande fiabilite permettant  
d'isoler des  
populations de cellules hematopoietiques enrichies en cellules souches,  
selectionnees en fonction de  
leur forte densite d'antigenes de surface des cellules CD34 (CD34hi).  
Les preparations a forte  
densite de cellules CD34 sont d'une grande utilite, par exemple, pour la  
recherche de nouveaux  
medicaments, pour la reconstitution de l'hematopoiese chez un animal  
presentant un dysfonctionnement  
du systeme hematopoietique et pour les therapies geniques.

L30 ANSWER 5 OF 5 USPATFULL on STN  
ACCESSION NUMBER: 97:99016 USPATFULL  
TITLE: Method for producing a highly enriched population of  
hematopoietic stem cells  
INVENTOR(S): DiGiusto, David, Palo Alto, CA, United States  
Galy, Anne, Palo Alto, CA, United States  
PATENT ASSIGNEE(S): Systemix, Inc., Palo Alto, CA, United States (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5681559		19971028
APPLICATION INFO.:	US 1995-474208		19950606 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1993-112603, filed on 25 Aug 1993, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Ziska, Suzanne E.		
LEGAL REPRESENTATIVE:	Morrison & Foerster LLP		
NUMBER OF CLAIMS:	17		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	40 Drawing Figure(s); 13 Drawing Page(s)		
LINE COUNT:	1339		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention provides a simple and reliable means for isolating  
populations of hematopoietic cells enriched for stem cell activity on  
the basis of possession of high CD34 cell surface antigen density

("CD34hi"). CD34.sup.hi cell preparations are useful, for example, for drug discovery efforts, for reconstituting hematopoiesis in an animal lacking a functioning hematopoietic system, and for gene therapies.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
L2 146532 S IN UTERO OR DONOR  
L3 59250 S PERCUTAN?  
L4 2 S L1 (S) L2 (S) 3  
L5 0 S L1 (S) L2 (S) L3  
L6 60 S L1 (S) L2  
L7 23472 S INCISION  
L8 0 S L1 (S) L2 (S) L7  
L9 354581 S TRANSPLANT?  
L10 14 S L1 (S) L2 (S) L9  
L11 1197155 S SUCTION OR VACUUM OR SUC?  
L12 1 S L1 (S) L2 (S) L9 (S) L11  
L13 1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?  
L14 1 S L1 (S) L2 (S) L9 (S) L13  
L15 247721 S ?CUTAN?  
L16 0 S L1 (S) L2 (S) L9 (S) L15  
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L22 59250 S PERCUTAN?  
L23 0 S L1 (S) L22  
L24 2 S L1 (L) L22  
L25 79 S L2 (S) L22  
L26 215420 S FETAL  
L27 8 S L2 (S) L22 (S) L26

FILE 'BIOSIS, EMBASE, CAPLUS, PCTFULL, USPATFULL, SCISEARCH, MEDLINE, CONFSCI' ENTERED AT 15:57:23 ON 20 JUL 2004

L28 80 S L14  
L29 69 DUP REM L28 (11 DUPLICATES REMOVED)  
L30 5 S L16

=> s 15

4 FILES SEARCHED...

L31 3 L5

=> d 1-3 ibib abs

L31 ANSWER 1 OF 3 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 1999267995 EMBASE  
TITLE: Successful expression of  $\beta$ -galactosidase and factor IX transgenes in fetal and neonatal sheep after ultrasound-guided percutaneous adenovirus vector administration into the umbilical vein.  
AUTHOR: Themis M.; Schneider H.; Kiserud T.; Cook T.; Adebakin S.; Jezard S.; Forbes S.; Hanson M.; Pavirani A.; Rodeck C.; Coutelle C.  
CORPORATE SOURCE: Prof. C. Coutelle, Cyst. Fibro. Gene Therapy Res. Group, Imp. College Science Technol. Med., Division of Biomedical Sciences, London SW7 2AZ, United Kingdom  
SOURCE: Gene Therapy, (1999) 6/7 (1239-1248).  
Refs: 33  
ISSN: 0969-7128 CODEN: GETHEC  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In **utero** somatic gene therapy in the later stages of pregnancy may allow targeting of organ systems which are difficult to reach later in life and to prevent the development of tissue damage otherwise caused by the early onset of inherited diseases. We report here on the **percutaneous** delivery of two adenoviral vectors, containing the  $\beta$ -galactosidase reporter gene and the human Factor IX gene respectively, to the fetal liver and circulation by ultrasound-guided umbilical vein puncture similar to procedures used in human pregnancy. Vector spread, as detected by PCR analysis for the  $\beta$ -galactosidase encoding vector, was found in almost all fetal and neonatal organs and in the maternal liver. Expression of the  $\beta$ -galactosidase transgene was detected in many fetal tissues by RT-PCR. High  $\beta$ -galactosidase production was shown by immuno-histochemistry predominantly in the liver, where about 30% of the hepatocytes stained positive, and in the adrenal cortex. Production of factor IX was determined by ELISA in the plasma of treated fetuses and newborn lambs and reached at birth up to 80% of the normal human plasma concentration. This demonstrates a very hopeful proof of principle for the development of prenatal treatment of many genetic diseases but also requires more detailed investigations with respect to the observed systemic spread of the vector.

L31 ANSWER 2 OF 3 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2001062891 PCTFULL ED 20020822

TITLE (ENGLISH): 207 HUMAN SECRETED PROTEINS

TITLE (FRENCH): 207 PROTEINES HUMAINES SECRETEES

INVENTOR(S): NI, Jian;  
EBNER, Reinhard;  
LAFLEUR, David, W.;  
MOORE, Paul, A.;  
OLSEN, Henrik, S.;  
ROSEN, Craig, A.;  
RUBEN, Steven, M.;  
SOPPET, Daniel, R.;  
YOUNG, Paul, E.;  
SHI, Yanggu;  
FLORENCE, Kimberly, A.;  
WEI, Ying-Fei;  
FLORENCE, Charles;  
HU, Jing-Shan;  
LI, Yi;  
KYAW, Hla;  
FISCHER, Carrie, L.;  
FERRIE, Ann, M.;  
FAN, Ping;  
FENG, Ping;  
ENDRESS, Gregory, A.;  
DILLON, Patrick, J.;  
CARTER, Kenneth, C.;  
BREWER, Laurie, A.;  
YU, Guo-Liang;  
ZENG, Zhizhen;  
GREENE, John, M.

PATENT ASSIGNEE(S): HUMAN GENOME SCIENCES, INC.;

NI, Jian;  
EBNER, Reinhard;  
LAFLEUR, David, W.;  
MOORE, Paul, A.;  
OLSEN, Henrik, S.;  
ROSEN, Craig, A.;  
RUBEN, Steven, M.;  
SOPPET, Daniel, R.;  
YOUNG, Paul, E.;  
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LI, Yi;

KYAW, Hla;  
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 FENG, Ping;  
 ENDRESS, Gregory, A.;  
 DILLON, Patrick, J.;  
 CARTER, Kennith, C.;  
 BREWER, Laurie, A.;  
 YU, Guo-Liang;  
 ZENG, Zhizhen;  
 GREENE, John, M.  
 Patent

DOCUMENT TYPE:  
 PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2001062891	A2	20010830
DESIGNATED STATES			
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2001-US5614	A	20010221
PRIORITY INFO.:	US 2000-60/184,836		20000224
	US 2000-60/193,170		20000329
ABEN	The present invention relates to the novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.		
ABFR	La presente invention concerne de nouvelles proteines humaines secretees ainsi que des acides nucleiques isoles contenant les regions codantes des genes codant ces proteines. L'invention concerne egalement des vecteurs, des cellules hotes, des anticorps ainsi que des methodes de recombinaison permettant la production de proteines humaines secretees. L'invention concerne egalement des methodes de diagnostic et therapeutiques utiles pour diagnostiquer et traiter des maladies, des troubles et/ou des etats lies a ces nouvelles proteines humaines secretees.		

L31 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 1999:543918 SCISEARCH

THE GENUINE ARTICLE: 213GP

TITLE: Successful expression of beta-galactosidase and factor IX transgenes in fetal and neonatal sheep after ultrasound-guided percutaneous adenovirus vector administration into the umbilical vein

AUTHOR: Themis M; Schneider H; Kiserud T; Cook T; Adebakin S; Jezard S; Forbes S; Hanson M; Pavirani A; Rodeck C; Coutelle C (Reprint)

CORPORATE SOURCE: UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED, CYST FIBROSIS GENE THERAPY RES GRP, DIV BIOMED SCI, LONDON SW7 2AZ, ENGLAND (Reprint); UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED, CYST FIBROSIS GENE THERAPY RES GRP, DIV BIOMED SCI, LONDON SW7 2AZ, ENGLAND; ROYAL FREE & UNIV COLL MED SCH, DEPT OBSTET & GYNAECOL, LONDON, ENGLAND; UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED, SCH MED, DEPT HISTOPATHOL, LONDON, ENGLAND; UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED, SCH MED, LIVER GRP LAB, LONDON, ENGLAND; TRANSGENE, STRASBOURG, FRANCE

COUNTRY OF AUTHOR: ENGLAND; FRANCE

SOURCE: GENE THERAPY, (JUL 1999) Vol. 6, No. 7, pp. 1239-1248. Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND. ISSN: 0969-7128.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 33

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB In utero somatic gene therapy in the later stages of pregnancy may allow targeting of organ systems which are difficult to reach later in life and to prevent the development of tissue damage otherwise caused by the early onset of inherited diseases. We report here on the percutaneous delivery of two adenoviral vectors, containing the beta-galactosidase reporter gene and the human Factor IX gene respectively, to the fetal liver and circulation by ultrasound-guided umbilical vein puncture similar to procedures used in human pregnancy. Vector spread, as detected by PCR analysis for the beta-galactosidase encoding vector, was found in almost all fetal and neonatal organs and in the maternal liver. Expression of the beta-galactosidase transgene was detected in many fetal tissues by RT-PCR. High beta-galactosidase production was shown by immuno-histochemistry predominantly in the liver, where about 30% of the hepatocytes stained positive, and in the adrenal cortex. Production of factor IX was determined by ELISA in the plasma of treated fetuses and newborn lambs and reached at birth up to 80% of the normal human plasma concentration. This demonstrates a very hopeful proof of principle for the development of prenatal treatment of many genetic diseases but also requires more detailed investigations with respect to the observed systemic spread of the vector.

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

L1 6659 S FETAL TISSUE  
L2 146532 S IN UTERO OR DONOR  
L3 59250 S PERCUTAN?  
L4 2 S L1 (S) L2 (S) 3  
L5 0 S L1 (S) L2 (S) L3  
L6 60 S L1 (S) L2  
L7 23472 S INCISION  
L8 0 S L1 (S) L2 (S) L7  
L9 354581 S TRANSPLANT?  
L10 14 S L1 (S) L2 (S) L9  
L11 1197155 S SUCTION OR VACUUM OR SUC?  
L12 1 S L1 (S) L2 (S) L9 (S) L11  
L13 1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?  
L14 1 S L1 (S) L2 (S) L9 (S) L13  
L15 247721 S ?CUTAN?  
L16 0 S L1 (S) L2 (S) L9 (S) L15  
L17 0 S L1 (L) L2 (L) L9 (L) L15  
L18 21 S L1 (L) L2 (L) L9 (L) L13  
L19 64 S L1 (L) L15  
L20 64 S L1 (L) L15 (L) L19  
L21 13 S L1 (L) L15 (L) L19 (L) L13  
L22 59250 S PERCUTAN?  
L23 0 S L1 (S) L22  
L24 2 S L1 (L) L22  
L25 79 S L2 (S) L22  
L26 215420 S FETAL  
L27 8 S L2 (S) L22 (S) L26

FILE 'BIOSIS, EMBASE, CAPLUS, PCTFULL, USPATFULL, SCISEARCH, MEDLINE, CONFSCI' ENTERED AT 15:57:23 ON 20 JUL 2004

L28 80 S L14  
L29 69 DUP REM L28 (11 DUPLICATES REMOVED)  
L30 5 S L16  
L31 3 S L5

=> s 112

4 FILES SEARCHED...

L32 74 L12

=> dup rem 132  
PROCESSING COMPLETED FOR L32  
L33 63 DUP REM L32 (11 DUPLICATES REMOVED)

=> d 1-63 ibib abs

L33 ANSWER 1 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2004048411 PCTFULL ED 20040615 EW 200424  
TITLE (ENGLISH): COMPOUNDS AND METHODS FOR MODULATING FUNCTIONS OF  
NONCLASSICAL CADHERINS  
TITLE (FRENCH): COMPOSES ET TECHNIQUES DESTINES A MODULER DES FONCTIONS  
DE CADHERINES NON CLASSIQUES  
INVENTOR(S): BLASCHUK, Orest, W., 4998 de Maisonneuve West, Suite  
1520, Westmount, Quebec H3Z 1N2, CA [CA, CA];  
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BLASCHUK, Orest, W., 4998 de Maisonneuve West, Suite  
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MICHAUD, Stephanie, D., 229 rue Gamelin, Hull, Quebec  
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Ontario K1P 1C3\$, CA  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
-----		
WO 2004048411	A2	20040610

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU  
ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA  
MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC  
SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN  
YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
MC NL PT RO SE SI SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2003-IB6208 A 20031114

PRIORITY INFO.: US 2002-60/426,551 20021114

US 2002-60/426,689 20021114

ABEN Modulating agents and methods for enhancing or inhibiting nonclassical  
cadherin-mediated functions, such as atypical or desmosomal cadherin  
-mediated functions, are provided. The modulating agents comprise at  
least a tryptophan-containing cell adhesion recognition sequence of an  
atypical and/or desmosomal cadherin, a conservative analogue or  
peptidomimetic thereof, or an antibody or fragment thereof that  
specifically binds to such a cell adhesion recognition sequence.  
Modulating agents may additionally comprise one or more cell adhesion  
recognition sequences recognized by cadherins and/or other adhesion  
molecules. Such modulating agents may, but need not, be linked to a  
targeting agent, pharmaceutically active substance and/or support  
material.

ABFR La presente invention concerne des agents de modulation et des  
techniques destinees a renforcer ou a inhiber des fonctions non  
classiques induites par la cadherine, telles que des fonctions induites  
par la cadherine atypiques ou desmosomales. Ces agents de modulation  
comprennent au moins une sequence de reconnaissance d'adhesion  
cellulaire contenant du tryptophane d'une cadherine atypique ou  
desmosomale, un analogue conservateur ou un peptidomimetique de celui-ci  
ou un anticorps ou un fragment de celui-ci qui se lie specifiquement a  
cette sequence de reconnaissance d'adhesion cellulaire. Des agents de  
modulation peuvent de plus comprendre une ou plusieurs sequences de

reconnaissance d'adhesion cellulaire reconnues par des cadherines et/ou par d'autres molecules d'adhesion. Ces agents de modulation peuvent, mais ce n'est pas obligatoire, etre lies a un agent de ciblage, a une substance pharmaceutiquement active et/ou a un materiau de support.

L33 ANSWER 2 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2004045592 PCTFULL ED 20040608 EW 200423  
TITLE (ENGLISH): COMPOUNDS AND METHODS FOR INCREASING NEUROGENESIS  
TITLE (FRENCH): COMPOSES ET METHODES PERMETTANT D'AUGMENTER LA  
NEUROGENESE  
INVENTOR(S): BERTILSSON, Goeran, Graensvaegen 5, S-137 41  
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Stockholm, SE [SE, SE], for all designates States  
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BERTILSSON, Goeran, Graensvaegen 5, S-137 41  
Vaesterhaninge, SE [SE, SE];  
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Biology, Medical Nobel Institute, Karolinska Institute,  
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HAEGESTRAND, Anders, Danaroevaegen 31, S-182 36  
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HEIDRICH, Jessica, Bolmensvaegen 12, S-120 50 Arsta, SE  
[SE, SE];  
HELLSTROEM, Kristina, Erikshaellsgatan 81, S-121 46  
Soedertaelje, SE [SE, SE];  
HAEGGBLAD, Johan, Vaestgoetagraend 21, S-118 28  
Vaestgoetagraend, SE [SE, SE];  
JANSSON, Katarina, Kalmagatan 28, S-121 45 Joanneshov,  
SE [SE, SE];  
KORTESMAA, Jarkko, Fatburs Brunnsgatan 27, S-118 28  
Stockholm, SE [SE, SE];



LINDQUIST, Per, Staltradsvaegen 21, S-168 68 Bromma, SE [SE, SE];  
 LUNDH, Hanna, Tunvaegen, S-170 68 Solna, SE [SE, SE];  
 MCGUIRE, Jacqueline, c/o Neuronova AB, Fiskartorpsvaegen 15A-D, S-114 33 Stockholm, SE [SE, SE];  
 MERCER, Alex, Staltradsvaegen 15, S-168 68 Bromma, SE [SE, SE];  
 NJBERG, Karl, Vacksalag 31B:1018, S-753 31 Uppsala, SE [SE, SE];  
 OSSOINAK, Amina, Tomtebogatan 38, S-113 38 Stockholm, SE [SE, SE];  
 PATRONE, Cesare, Haegerstenvaegen 111, S-126 49 Haegersten, SE [SE, SE];  
 ROENNHOLM, Harriet, Tornslingan 8, 1tr, S-142 61 Trangsund, SE [SE, SE];  
 ZACHRISSON, Olof, Kaelvestavaegen 65, S-163 54 Spanga, SE [SE, SE];  
 WIKSTROEM, Lilian, Stjaernfallsvaegen 9, S-163 54 Spanga, SE [SE, SE];  
 E. BLUM & CO.\$, Vorderberg 11, CH-8044 Zuerich\$, CH

AGENT:  
 LANGUAGE OF FILING:  
 LANGUAGE OF PUBL.:  
 DOCUMENT TYPE:  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2004045592	A2	20040603

# DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO  
 CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR  
 HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV  
 MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU  
 SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC  
 VN YU ZA ZM ZW

RW (ARIPO):

BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO):

AM AZ BY KG KZ MD RU TJ TM

RW (EPO):

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
 MC NL PT RO SE SI SK TR

RW (OAPI):

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2003-IB5311 A 20031120

PRIORITY INFO.:

US 2002-60/427,912 20021120

ABEN

The invention is directed to methods of promoting neurogenesis by contacting neuronal tissue with intracellular cAMP elevating agents and intracellular Ca<sup>2+</sup> elevating agents. Novel agents for promoting neurogenesis are disclosed. These agents include novel agents for increasing intracellular cAMP.

ABFR

L'invention concerne des methodes permettant de promouvoir la neurogenese par mis en contact d'un tissu neural avec des agents d'elevation de niveau intracellulaire de cAMP et de Ca<sup>2+</sup>. L'invention concerne de nouveaux agents permettant de promouvoir la neurogenese, ces agents permettant d'augmenter le niveau intracellulaire de cAMP.

L33 ANSWER 3 OF 63

ACCESSION NUMBER:

PCTFULL COPYRIGHT 2004 Univentio on STN  
 2004044000 PCTFULL ED 20040602 EW 200422

TITLE (ENGLISH):

COMPOUNDS AND METHODS FOR MODULATING FUNCTIONS OF  
 CLASSICAL CADHERINS

TITLE (FRENCH):

COMPOSES ET PROCEDES DE MODULATION DE FONCTIONS DE  
 CADHERINES CLASSIQUES

INVENTOR(S):

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 designates States except US;  
 BLASCHUK, Orest, W., Suite 1520, 4998 de Maisonneuve  
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 MICHAUD, Stephanie, Denise, 229 rue Gamelin, Hull,

AGENT: Quebec J8Y 1W5, CA [CA, CA], for US only  
DE KOCK, Elbie, R.\$, Russell Reyneke, Suite 700, Two  
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Columbia V7X 1M8\$, CA  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2004044000	A2	20040527

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO  
CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR  
HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV  
MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU  
SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC  
VN YU ZA ZM ZW  
RW (ARIPO): BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
MC NL PT RO SE SI SK TR  
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2003-CA1746 A 20031114  
PRIORITY INFO.: US 2002-60/426,194 20021114

ABEN Modulating agents and methods for enhancing or inhibiting classical  
cadherin-mediated functions are provided. The modulating agents comprise  
at least a tryptophan-containing cell adhesion recognition sequence of a  
classical cadherin molecule, a conservative analogue or peptidomimetic  
thereof, or an antibody or fragment thereof that specifically binds to  
such a cell adhesion recognition sequence. Modulating agents may  
additionally comprise one or more cell adhesion recognition sequences  
recognized by cadherins and/or other adhesion molecules. Such modulating  
agents may, but need not, be linked to a targeting agent,  
pharmaceutically active substance and/or support material.

ABFR L'invention concerne des agents et des procedes de modulation permettant  
d'ameliorer ou d'inhiber des fonctions regulees par des cadherines  
classiques. Ces agents de modulation comprennent au moins une sequence  
de reconnaissance d'adhesion de cellules contenant tryptophane d'une  
molecule de cadherine classique, un analogue conservatif ou un  
peptidomimetique de cette sequence, ou un anticorps ou un fragment  
d'anticorps de cette sequence qui se lie specifiquement a cette sequence  
de reconnaissance d'adhesion de cellules. Des agents de modulation  
peuvent comprendre en plus une ou plusieurs sequences de reconnaissance  
d'adhesion de cellules reconnues par les cadherines et/ou par d'autres  
molecules d'adhesion. Ces agents de modulation peuvent, eventuellement,  
etre lies a un agent de ciblage, a une substance pharmaceutiquement  
active et/ou a une matiere de support.

L33 ANSWER 4 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2004016772 PCTFULL ED 20040302 EW 200409  
TITLE (ENGLISH): A METHOD OF CELL RE-PROGRAMMING BY CYTOPLASMIC TRANSFER  
TITLE (FRENCH): PROCEDE DE REPROGRAMMATION CELLULAIRE PAR TRANSFERT  
CYTOPLASMIQUE

INVENTOR(S): NIEHRS, Christof, Klingenteichstrasse 6b, 69117  
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OeffENTLICHEN RECHTS, Im Neuenheimer Feld 280, 69120  
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NIEHRS, Christof, Klingenteichstrasse 6b, 69117  
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HANSIS, Christoph, Humboldtstrasse 17, 53115 Bonn, DE  
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AGENT: HUHN, Michael\$, Isenbruck, Boesl, Hoerschler, Wichmann,  
Huhn, Theodor-Heuss-Anlage 12, 68165 Mannheim\$, DE  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent

## PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2004016772	A1	20040226
DESIGNATED STATES			
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW		
RW (ARIPO):	GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW		
RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM		
RW (EPO):	AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR		
RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2003-EP8930	A	20030812
PRIORITY INFO.:	EP 2002-02018014.7		20020812
ABEN	The present invention refers to a method for reprogramming a recipient cell, the method comprising, first, contacting the recipient cell with the cytoplasm of a donor cell from an amphibian or from a bony fish and, second, detecting the expression of embryonic markers in the recipient cell. Furthermore, the present invention contemplates the therapeutic use of the disclosed method for diseases requiring the replacement or renewal of cells.		
ABFR	La presente invention concerne un procede permettant de reprogrammer une cellule receptrice. La 1<sp>ere</sp> operation de ce procede consiste en une mise en contact de la cellule receptrice avec le cytoplasme d'une cellule donneuse prelevee sur un amphibien ou un poisson osseux. La 2<sp>eme</sp> operation consiste en une detection de l'expression de marqueurs embryonnaires dans la cellule receptrice. L'invention concerne egalement concerne egalement l'utilisation therapeutique des procedes de l'invention pour des maladies necessitant le remplacement ou le renouvellement de cellules.		

L33 ANSWER 5 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2004275182 EMBASE  
TITLE: Is there a future for neural transplantation?.  
AUTHOR: Narrower T.P.; Barker R.A.  
CORPORATE SOURCE: Dr. T.P. Narrower, Cambridge Centre for Brain Repair,  
Forvie Site, Robinson Way, Cambridge CB22PY, United  
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SOURCE: BioDrugs, (2004) 18/3 (141-153).  
Refs: 141  
ISSN: 1173-8804 CODEN: BIDRF4  
COUNTRY: New Zealand  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 008 Neurology and Neurosurgery  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Traditionally neural transplantation has had as its central tenet the replacement of missing neurons that have been lost because of neurodegenerative processes, as exemplified by diseases such as Parkinson disease (PD). However, the effectiveness and widespread application of this approach clinically has been limited, primarily because of the poor donor supply of human fetal neural tissue and the incomplete neurobiological understanding of the circuit reconstruction required to normalize function in these diseases. So, in PD the progress from promising neural transplantation in animal models to proof-of-principle, open-labeled clinical transplants, to randomized, placebo-controlled studies of neural transplantation has not been straightforward. The emergence of previously undescribed adverse effects and lack of significant functional advantage in recent clinical studies has been disappointing and has served to cast a new, and perhaps more realistic, perspective on this treatment approach. In fact, there have been calls by some involved in neural transplantation to return to the drawing board before pressing on with further clinical trials, and the return to basic experimentation.

This therefore precipitates the question - is there a future for neural transplantation? It is important to remember that there are a number of possible explanations for the disappointing results from the recent clinical trials in PD, ranging from the mode of transplantation to patient selection. Nevertheless, almost irrespective of these reasons for the current trial results, there have always been significant practical and ethical problems with using human fetal tissue, and so a number of alternative cell sources have been investigated. These alternative sources include stem cells, which are attractive for cell-based therapies because of their potential ease of isolation, propagation and manipulation, and their ability in some cases to migrate to areas of pathology and differentiate into specific and appropriate cell types. Furthermore, the availability of stem cells derived from non-embryonic sources (e.g. adult stem cells derived from the sub-ventricular zone) has removed some of the ethical limitations associated with the use of embryonic human tissue. These potentially beneficial aspects of stem cells means that there is a future for neural transplantation as a means of treating patients with a range of neurological disorders, although whether this will ever translate into a truly effective, widely available therapy remains unknown.

L33 ANSWER 6 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2003094965 PCTFULL ED 20031125 EW 200347  
 TITLE (ENGLISH): MODULATION OF NEURAL STEM CELLS AND NEURAL PROGENITOR CELLS  
 TITLE (FRENCH): MODULATION DE CELLULES SOUCHES NEURALES ET DE CELLULES PROGENITRICES NEURALES  
 INVENTOR(S): LINDQUIST, Per, Staltrtadsvagen 21, S-168 68 Bromma, SE [SE, SE];  
 MERCER, Alex, Staltrtadsvagen 15, S-168 68 Bromma, SE [SE, SE];  
 RONNHOLM, Harriet, Tornslingsan 8, 1 tr, S-142 61 Trangsund, SE [SE, SE];  
 WIKSTROM, Lilian, Stjarnfallsvagen 9, S-163 54 Spanga, SE [SE, SE]  
 PATENT ASSIGNEE(S): NEURONOVA AB, Fiskartorpsvagen15A-D, S-114 33 Stockholm, SE [SE, SE], for all designates States except US;  
 LINDQUIST, Per, Staltrtadsvagen 21, S-168 68 Bromma, SE [SE, SE], for US only;  
 MERCER, Alex, Staltrtadsvagen 15, S-168 68 Bromma, SE [SE, SE], for US only;  
 RONNHOLM, Harriet, Tornslingsan 8, 1 tr, S-142 61 Trangsund, SE [SE, SE], for US only;  
 WIKSTROM, Lilian, Stjarnfallsvagen 9, S-163 54 Spanga, SE [SE, SE], for US only  
 AGENT: MACLEAN, Martin, Robert\$, Mathys & Squire, 100 Gray's Inn Road, London WC1X 8AL\$, GB  
 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003094965	A2	20031120

DESIGNATED STATES

W:

AE	AG	AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	BZ	CA	CH	CN	CO	CR	CU	CZ	DE	DK	DM	DZ	EC	EE	ES	FI	GB	GD	GE	GH	GM	HR	HU	ID	IL	IN	IS	JP	KE	KG	KP	KR	KZ	LC	LK	LR	LS	LT	LU	LV	MA	MD	MG	MK	MN	MW	MX	MZ	NI	NO	NZ	OM	PH	PL	PT	RO	RU	SC	SD	SE	SG	SK	SL	TJ	TM	TN	TR	TT	TZ	UA	UG	US	UZ	VC	VN	YU	ZA	ZM	ZW
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RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
 RW (EAP): AM AZ BY KG KZ MD RU TJ TM  
 RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PT RO SE SI SK TR  
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2003-IB2370 A 20030508  
 PRIORITY INFO.: US 2002-60/379,114 20020508  
 US 2002-60/393,159 20020702

ABEN The invention relates generally to methods of influencing central nervous system cells to produce progeny useful in the treatment of CNS disorders. More specifically, the invention includes methods of exposing a patient suffering from such a disorder to a reagent that modulates the proliferation, migration, differentiation and survival of central nervous system cells via S1P or LPA signaling. These methods are useful for reducing at least one symptom of the disorder.

ABFR L'invention concerne generalement des procedes permettant d'influencer les cellules du systeme nerveux central afin de produire des progeniteurs utiles dans le traitement de troubles du SNC. Elle concerne plus specifiquement des procedes d'exposition d'un patient souffrant d'un tel trouble a un reactif qui module la proliferation, la migration, la differentiation et la survie de cellules du systeme nerveux central via une signalisation S1P ou LPA. Ces procedes sont utiles afin de reduire au moins un symptome du trouble.

L33 ANSWER 7 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2003092716 PCTFULL ED 20031118 EW 200346  
TITLE (ENGLISH): THE FUNCTIONAL ROLE AND POTENTIAL THERAPEUTIC USE OF PACAP, VIP AND MAXADILAN IN RELATION TO ADULT NEURAL STEM OR PROGENITOR CELLS  
TITLE (FRENCH): ROLE FONCTIONNEL ET UTILISATION THERAPEUTIQUE POTENTIELLE DE PACAP, VIP ET MAXADILAN EN RAPPORT AVEC DES CELLULES PROGENITRICES OU SOUCHES NEURONALES CHEZ L'ADULTE  
INVENTOR(S): MERCER, Alex, Stalradsvagen 15, SE-168 68 Bromma, SE [SE, SE];  
PATRONE, Cesare, Hagerstensvagen 11, SE-126 49 Hagersten, SE [SE, SE];  
RONNHOLM, Harriet, Tornslingan 8, 1 tr., SE-142 61 Trangsund, SE [SE, SE];  
WIKSTROM, Lilian, Stjarnfallsvagen 90, SE-163 54 Spanga, SE [SE, SE]  
PATENT ASSIGNEE(S): NEURONOVA AB, Fiskartorpsvagen 15A-D, SE-114 33 Stockholm, SE [SE, SE], for all designates States except US;  
MERCER, Alex, Stalradsvagen 15, SE-168 68 Bromma, SE [SE, SE], for US only;  
PATRONE, Cesare, Hagerstensvagen 11, SE-126 49 Hagersten, SE [SE, SE], for US only;  
RONNHOLM, Harriet, Tornslingan 8, 1 tr., SE-142 61 Trangsund, SE [SE, SE], for US only;  
WIKSTROM, Lilian, Stjarnfallsvagen 90, SE-163 54 Spanga, SE [SE, SE], for US only  
AGENT: MACLEAN, Martin, Robert\$, Mathys & Squire, 100 Gray's Inn Road, London WC1X 8AL\$, GB  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003092716	A2	20031113

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID  
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE  
SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM  
ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU  
MC NL PT RO SE SI SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2003-IB2167 A 20030502

PRIORITY INFO.: US 2002-60/377,734 20020503

US 2002-60/393,264 20020702

US 2002-60/426,827 20021115

ABEN The invention relates generally to methods of influencing central nervous system cells to produce progeny useful in the treatment of CNS

disorders. More specifically, the invention includes methods of exposing a patient suffering from such a disorder to a reagent that modulates the proliferation, migration, differentiation and survival of central nervous system cells via PACAP, Maxadilan or VIP signaling. These methods are useful for reducing at least one symptom of the disorder.

ABFR L'invention concerne d'une maniere generale des procedes pour influencer les cellules du systeme nerveux central afin de produire une progeniture utile dans le traitement de troubles du SNC. Elle concerne plus particulierement des procedes pour exposer un patient souffrant d'un de ces troubles a un reactif qui module la proliferation, la migration, la differentiation et la survie des cellules du systeme nerveux central via la signalisation PACAP, Maxadilan ou VIP. Ces procedes sont utiles pour reduire au moins un symptome du trouble en question.

L33 ANSWER 8 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2003066120 PCTFULL ED 20030828 EW 200333  
 TITLE (ENGLISH): TREATING DEGENERATIVE DISC DISEASE THROUGH  
 TRANSPLANTATION OF ALLOGRAFT DISC  
 TITLE (FRENCH): TRAITEMENT D'UNE MALADIE DEGENERATIVE DU DISQUE PAR  
 TRANSPLANTATION D'UN DISQUE ALLOGREFFE  
 INVENTOR(S): FERREE, Bret, A., 1238 Cliff Laine Drive, Cincinnati,  
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 LANGUAGE OF FILING: English  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003066120	A1	20030814

#### DESIGNATED STATES

W: AU CA JP  
 RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 TR

APPLICATION INFO.: WO 2002-US3123 A 20020204

ABEN The intervertebral disc and a portion of adjacent vertebrae obtained from recently deceased human or animal donors are used to restore disc function and eliminate pain in patients with disc disease. Cells harvested and cultured from the nucleus pulposus and/or the annulus fibrosis of a normal disc are added to the donor disc. Additional therapeutic substances like culture medium, growth factors, differentiation factors, hydrogels polymers, antibiotics, anti-inflammatory medications, or immunosuppressive medications may also be added to the transplanted disc unit.

ABFR On utilise le disque intervertebral et une partie de vertebre contigue obtenue d'un donneur humain recemment decede ou d'un donneur animal pour restaurer la fonction du disque et eliminer les douleurs ressenties par des patients atteints d'une maladie du disque. Des cellules recueillies et cultivees du noyau gelatineux et/ou de l'anneau fibreux d'un disque normal sont ajoutees au disque du donneur. On peut aussi ajouter au disque transplante des substances therapeutiques additionnelles comme un milieu de culture, des facteurs de croissance, des facteurs de differentiation, des polymeres hydrogels, des antibiotiques, des medications anti-inflammatoires des medications immunodepressives.

L33 ANSWER 9 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2003047635 PCTFULL ED 20030620 EW 200324  
 TITLE (ENGLISH): USE OF CD34+ HEMATOPOIETIC PROGENITOR CELLS FOR THE  
 TREATMENT OF CNS DISORDERS  
 TITLE (FRENCH): UTILISATION DES CELLULES HEMATOPOIETIQUES CD34+ DANS LE  
 TRAITEMENT DES TROUBLES SNC  
 INVENTOR(S): CARTIER-LACAVE, Nathalie, 68, rue de Rivoli, F-75004  
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Boulogne-Billancourt, FR [FR, FR], for US only;  
ASHUEUR, Muriel, 1, rue Bauges, F-75016 Paris, FR [FR,  
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PFLUMIO, Françoise, 47, voie Houdon, F-94400 Vitry sur  
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LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 2003047635	A1	20030612
DESIGNATED STATES			
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW		
RW (ARIPO):	GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW		
RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM		
RW (EPO):	AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SI SK TR		
RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG		
APPLICATION INFO.:	WO 2002-IB5698	A	20021206
PRIORITY INFO.:	US 2001-60/337,078		20011206

ABEN The present invention provides novel methods for delivering cells,  
particularly modified

cells, to the central nervous system (CNS). The purpose of this  
invention is to

present a method that provides sustained delivery of a molecule to the  
central nervous

system, thereby increasing the bioavailability of the molecule and  
lengthening

the possible duration of treatment.

ABFR L'invention se rapporte a de nouvelles methodes d'administration de  
cellules, notamment des cellules modifiees, au systeme nerveux central  
(SNC). L'invention repose sur une methode qui assure une administration  
reguliere d'une molecule au systeme nerveux central,  
ce qui permet d'augmenter la biodisponibilite de la molecule  
et d'allonger la duree possible du traitement.

L33 ANSWER 10 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2003039575 PCTFULL ED 20030520 EW 200320  
TITLE (ENGLISH): THE FUNCTIONAL ROLE AND POTENTIAL THERAPEUTIC USE OF  
REELIN, GAS6 AND PROTEIN S IN RELATION TO ADULT NEURAL  
STEM OR PROGENITOR CELLS  
TITLE (FRENCH): ROLE FONCTIONNEL ET UTILISATION THERAPEUTIQUE  
POTENTIELLE DE PROTEINES S, GAS6 ET REELIN EN RELATION  
AVEC DES CELLULES SOUCHES NEURONALES ADULTES

INVENTOR(S): BERTILSSON, Goran, Grasnvagen 5, S-137 41  
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KORTESMAA, Jarkko, Fatburs Brunnsgatan 27, S-118 28  
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PATRONE, Cesare, Haegerstensvaegen 111, S-126 49  
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PATENT ASSIGNEE(S): NEURONOVA AB, Fiskartorpsvagen 15A-D, S-114 33  
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FRISEN, Jonas, Brahegatan 19, S-114 37 Stockholm, SE  
[SE, SE], for US only;  
FALK, Anna, Gustav III:s Boulevard 3, S-169 72 Solna,  
SE [SE, SE], for US only;  
HEIDRICH, Jessica, Bolmensvaegen 12, S-120 50 Arsta, SE  
[SE, SE], for US only;  
HELLSTROM, Kristina, Erikhaellsgatan 81, S-151 46  
Sodertaelje, SE [SE, SE], for US only;  
KORTESMAA, Jarkko, Fatburs Brunnsgatan 27, S-118 28  
Stockholm, SE [FI, SE], for US only;  
LINDQUIST, Per, Staltradsvaegen 21, S-168 68 Bromma, SE  
[SE, SE], for US only;  
LUNDH, Hanna, Tunvaegen 13, S-170 68 Solna, SE [SE,  
SE], for US only;  
MCGUIRE, Jaccqueline, Stationsvaegen 45, S-141 40  
Huddinge, SE [GB, SE], for US only;  
MERCER, Alex, Staltradsvaegen 15, S-168 68 Bromma, SE  
[GB, SE], for US only;  
PATRONE, Cesare, Haegerstensvaegen 111, S-126 49  
Hagersten, SE [IT, SE], for US only;  
RONNHOLM, Harriet, Tornslingsan 8, 1 tr., S-142 61  
Trangsund, SE [FI, SE], for US only;  
WIKSTROM, Lilian, Stjaernfallsvaegen 9, S-163 54  
Spanga, SE [FI, SE], for US only;  
ZACHRISSON, Olof, Kaelvestavaegen 65, S-163 54 Spanga,  
SE [SE, SE], for US only

AGENT: MACLEAN, Martin, Robert\$, Mathys & Squire, 100 Gray's  
Inn Road, London WC1X 8AL\$, GB

LANGUAGE OF FILING: English

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003039575	A2	20030515

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID



IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG  
SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM  
ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC  
NL PT SE SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-GB5078 A 20021111  
PRIORITY INFO.: US 2001-60/344,725 20011109  
US 2001-60/345,064 20011109  
US 2002-60/393,263 20020702  
US 2002-60/394,397 20020708

ABEN The invention relates generally to methods of influencing central  
nervous system  
cells to produce progeny useful in the treatment of CNS disorders. More  
specifically,  
the invention includes methods of exposing a patient suffering from such  
a disorder  
to reagent that modulates the proliferation, migration, differentiation  
and  
survival of central nervous system cells via Reelin, Gas6 or Protein S  
signaling.  
These methods are useful for reducing at least one symptom of the  
disorder.

ABFR L'invention concerne de maniere generale des procedes  
destines a influencer des cellules du systeme nerveux central  
afin d'obtenir une descendance utile dans le traitement des troubles du  
SNC. Plus particulierement, l'invention comprend des procedes  
destines a exposer un patient souffrant dudit trouble a un reactif  
qui module la proliferation, la migration, la differentiation et  
la survie des cellules du systeme nerveux central par l'intermediaire  
d'une signalisation de proteines Reelin, Gas6 ou S. Ces procedes  
sont utiles pour reduire au moins un symptome dudit trouble.

L33 ANSWER 11 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2003014317 PCTFULL ED 20030303 EW 200308  
TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR ISOLATION, PROPAGATION,  
AND DIFFERENTIATION OF HUMAN STEM CELLS AND USES  
THEREOF  
TITLE (FRENCH): COMPOSITIONS ET PROCEDES PERMETTANT D'ISOLER DE FAIRE  
PROLIFERER ET DE DIFFERENCIER DES CELLULES-SOUCHES  
HUMAINES ET UTILISATION DE CELLES-CI  
INVENTOR(S): NEUMAN, Toomas, 209 Montana Avenue, Apt # 201, Santa  
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LEVESQUE, Michel, 457 South Camden Drive, Beverly  
Hills, CA 90212, US  
PATENT ASSIGNEE(S): CELMED BIOSCIENCES USA, 110 George Burns Road, Suite  
4090, Los Angeles, CA 90048, US [US, US]  
AGENT: ALTMAN, Daniel, E.\$, Knobbe, Martens, Olson & Bear,  
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92614\$, US  
LANGUAGE OF FILING: English  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2003014317	A2	20030220

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID  
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI  
SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC  
NL PT SE SK TR  
RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-US25191 A 20020808  
PRIORITY INFO.: US 2001-60/310,727 20010808  
US 2001-60/312,714 20010816

ABEN The invention is directed to the field of human stem cells and includes methods and compositions for isolating, propagating, and differentiating human stem cells. The invention provides therapeutic uses of the methods and compositions, including autologous transplantation of treated cells into humans for treatment of Parkinson's and other neuronal disorders.

ABFR Cette invention, qui relève du domaine des cellules-souches humaines, a trait a des procedes et aux compositions afferentes permettant d'isoler, de faire proliferer et de differencier des cellules-souches humaines. Elle porte egalement sur des utilisations therapeutiques de ces compositions et des procedes susmentionnes, notamment en matiere de transplantation autologue de cellules traitees chez des patients humains aux fins du traitement de la maladie de Parkinson et d'autres troubles neuroaux.

L33 ANSWER 12 OF 63 USPATFULL on STN

ACCESSION NUMBER: 2003:172722 USPATFULL  
TITLE: Compositions and methods for isolation, propagation, and differentiation of human stem cells and uses thereof  
INVENTOR(S): Neuman, Toomas, Santa Monica, CA, UNITED STATES  
Levesque, Michel, Beverly Hills, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003118566	A1	20030626
APPLICATION INFO.:	US 2002-216677	A1	20020808 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-310727P	20010808 (60)
	US 2001-312714P	20010816 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET, FOURTEENTH FLOOR, IRVINE, CA, 92614	
NUMBER OF CLAIMS:	33	
EXEMPLARY CLAIM:	1	
LINE COUNT:	1836	

AB The invention is directed to the field of human stem cells and includes methods and compositions for isolating, propagating, and differentiating human stem cells. The invention provides therapeutic uses of the methods and compositions, including autologous transplantation of treated cells into humans for treatment of Parkinson's and other neuronal disorders.

L33 ANSWER 13 OF 63 USPATFULL on STN

ACCESSION NUMBER: 2003:279262 USPATFULL  
TITLE: Nuclear transfer using cells cultured in serum starvation media containing apoptosis inhibitors  
INVENTOR(S): Piedrahita, Jorge A., College Station, TX, United States  
Lee, Chang-Kyu, Suwon, KOREA, REPUBLIC OF  
Weeks, Regina, Richardson, TX, United States  
Bazer, Fuller, College Station, TX, United States  
PATENT ASSIGNEE(S): The Texas A&M University System, College Station, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6635802	B1	20031021
APPLICATION INFO.:	US 2001-758024		20010110 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-175196P	20000110 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Crouch, Deborah	

LEGAL REPRESENTATIVE: Bracewell & Patterson LLP  
NUMBER OF CLAIMS: 60  
EXEMPLARY CLAIM: 58  
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 5 Drawing Page(s)  
LINE COUNT: 2868

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided are methods and compositions for increasing the efficiency of nuclear transfer using apoptosis inhibitors, and for the production of transgenic and non-transgenic mammals from cultured cells or cell lines. Methods for cloning mammals, and for producing transgenic and chimeric mammalian tissues and mammals, and chimeric cell lines are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L33 ANSWER 14 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003421710 EMBASE  
TITLE: Engraftment and tumor formation after allogeneic in utero transplantation of primate embryonic stem cells.  
AUTHOR: Asano T.; Ageyama N.; Takeuchi K.; Momoeda M.; Kitano Y.; Sasaki K.; Ueda Y.; Suzuki Y.; Kondo Y.; Torii R.; Hasegawa M.; Ookawara S.; Harii K.; Terao K.; Ozawa K.; Hanazono Y.  
CORPORATE SOURCE: Dr. Y. Hanazono, Division of Regenerative Medicine, Center for Molecular Medicine, Jichi Medical School, 3311-1 Yakushi-ji, Kawachi, Tochigi 329-0498, Japan.  
hanazono@jichi.ac.jp  
SOURCE: Transplantation, (15 Oct 2003) 76/7 (1061-1067).  
Refs: 27  
ISSN: 0041-1337 CODEN: TRPLAU  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 025 Hematology  
026 Immunology, Serology and Transplantation  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Background. To achieve human embryonic stem (ES) cell-based **transplantation** therapies, allogeneic **transplantation** models of nonhuman primates would be useful. We have prepared cynomolgus ES cells genetically marked with the green fluorescent protein (GFP). The cells were **transplanted** into the allogeneic fetus, taking advantage of the fact that the fetus is so immunologically immature as not to induce immune responses to **transplanted** cells and that **fetal tissue** compartments are rapidly expanding and thus providing space for the engraftment. Methods. Cynomolgus ES cells were genetically modified to express the GFP gene using a simian immunodeficiency viral vector or electroporation. These cells were **transplanted** in utero with ultrasound guidance into the cynomolgus fetus in the abdominal cavity (n=2) or liver (n=2) at the end of the first trimester. Three fetuses were delivered 1 month after **transplantation**, and the other, 3 months after **transplantation**. Fetal tissues were examined for **transplanted** cell progeny by quantitative polymerase chain reaction and in situ polymerase chain reaction of the GFP sequence. Results. A fluorescent tumor, obviously derived from **transplanted** ES cells, was found in the thoracic cavity at 3 months after **transplantation** in one fetus. However, **transplanted** cell progeny were also detected (~ 1%) without teratomas in multiple **fetal tissues**. The cells were solitary and indistinguishable from surrounding host cells. Conclusions. **Transplanted** cynomolgus ES cells can be engrafted in allogeneic fetuses. The cells will, however, form a tumor if they "leak" into an improper space such as the thoracic cavity.

L33 ANSWER 15 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 1

ACCESSION NUMBER: 2003464769 EMBASE  
TITLE: Staging and Preparation of Human Fetal Striatal Tissue for Neural Transplantation in Huntington's Disease.  
AUTHOR: Rosser A.E.; Barker R.A.; Armstrong R.J.E.; Elneil S.; Jain M.; Hurelbrink C.B.; Prentice A.; Carne C.; Thornton S.;

Hutchinson H.; Dunnett S.B.

CORPORATE SOURCE: A.E. Rosser, School of Biosciences, Cardiff University,  
Museum Avenue, Cardiff CF10 3US, United Kingdom.  
RosserAE@cf.ac.uk

SOURCE: Cell Transplantation, (2003) 12/7 (679-686).  
Refs: 38  
ISSN: 0963-6897 CODEN: CTRAE8

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology  
008 Neurology and Neurosurgery  
021 Developmental Biology and Teratology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB **Transplantation** of human fetal central nervous system tissue has been shown to be of benefit in Parkinson's disease, and is currently being explored as a therapeutic option in Huntington's disease. The **success** of a neural transplant is dependent on a number of factors, including the requirement that **donor** cells are harvested within a given developmental window and that the cell preparation protocols take account of the biological parameters identified in animal models. Although many of the criteria necessary for a **successful** neural transplant have been defined in animal models, ultimately they must be validated in human studies, and some issues can only ever be addressed in human studies. Furthermore, because neural **transplantation** of human **fetal tissue** is limited to small numbers of patients in any one surgical center, largely due to practical constraints, it is crucial that tissue preparation protocols are clearly defined and reproducible, so that (i) multicenter trials are possible and are based on consistent tissue preparation parameters, and (ii) results between centers can be meaningfully analyzed. Here we describe the preparation of human fetal striatum for neural **transplantation** in Huntington's disease, and report on the validation of a method for estimating the developmental stage of the fetus based on direct morphometric measurements of the embryonic tissue.

L33 ANSWER 16 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2002051997 PCTFULL ED 20020716 EW 200227

TITLE (ENGLISH): METHODS FOR CLONING MAMMALS USING REPROGRAMMED DONOR CHROMATIN OR DONOR CELLS

TITLE (FRENCH): METHODES DE CLONAGE DE MAMMIFERES A L'AIDE DE CHROMATINE DONNEUSE REPROGRAMMEE OU DE CELLULES DONNEUSES REPROGRAMMEES

INVENTOR(S): COLLAS, Philippe, Nygaardsalle 4A, N-0871 Oslo, NO [FR, NO];  
ROBL, James, M., 196 Old Enfield Road, Belchertown, MA 01007, US [US, US];  
SULLIVAN, Eddie, 2937 Dimrill Stair, Manhattan, KS 66503, US [US, US];  
KASINATHAN, P., 1540 Waterford Place #1, Manhattan, KS 66502, US [LK, US]

PATENT ASSIGNEE(S): AUROX LLC, 33 Riverside Avenue, 2nd Floor, Westport, CT 06880, US [US, US], for all designates States except US;  
COLLAS, Philippe, Nygaardsalle 4A, N-0871 Oslo, NO [FR, NO], for US only;  
ROBL, James, M., 196 Old Enfield Road, Belchertown, MA 01007, US [US, US], for US only;  
SULLIVAN, Eddie, 2937 Dimrill Stair, Manhattan, KS 66503, US [US, US], for US only;  
KASINATHAN, P., 1540 Waterford Place #1, Manhattan, KS 66502, US [LK, US], for US only

AGENT: ELBING, Karen, L.\$, Clark & Elbing LLP, 176 Federal Street, Boston, MA 02110-2214\$, US

LANGUAGE OF FILING: English

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
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WO 2002051997 A1 20020704

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR  
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID  
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD  
MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL  
TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW  
RW (EAPO): AM AZ BY KG KZ MD RU TJ TM  
RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US50406 A 20011221

PRIORITY INFO.: US 2000-60/258,151 20001222

ABEN The invention provides methods for cloning mammals that allow the donor chromosomes or donor cells to be reprogrammed prior to insertion into an enucleated oocyte. The invention also features methods of inserting chromosomes or nuclei into recipient cells.

ABFR La presente invention concerne des methodes de clonage de mammiferes permettant la reprogrammation de cellules donneuses ou de chromosomes donneurs avant leur introduction dans un ovocyte enuclee. Cette invention concerne egalement des procedes permettant d'introduire des chromosomes ou des noyaux dans des cellules receptrices.

L33 ANSWER 17 OF 63 USPATFULL on STN

ACCESSION NUMBER: 2002:75643 USPATFULL

TITLE: Methods comprising apoptosis inhibitors for the generation of transgenic pigs

INVENTOR(S): Piedrahita, Jorge A., College Station, TX, United States

Bazer, Fuller W., College Station, TX, United States  
PATENT ASSIGNEE(S): Texas A&M University System, College Station, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6369294	B1	20020409
	US 2002045253	A1	20020418
APPLICATION INFO.:	US 2001-819964		20010328 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1997-949155, filed on 10 Oct 1997, now patented, Pat. No. US 6271436		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-46094P	19970509 (60)
	US 1996-27338P	19961011 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Crouch, Deborah

ASSISTANT EXAMINER: Pappu, Sita

LEGAL REPRESENTATIVE: Bracewell & Patterson L.L.P.

NUMBER OF CLAIMS: 58

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)

LINE COUNT: 9398

AB Disclosed are methods for the isolation of primordial germ cells, culturing these cells to produce primordial germ cell-derived cell lines, methods for transforming both the primordial germ cells and the cultured cell lines, and using these transformed cells and cell lines to generate transgenic animals. The efficiency at which transgenic animals are generated by the present invention is greatly increased, thereby allowing the use of homologous recombination in producing transgenic non-rodent animal species.

L33 ANSWER 18 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2001062891 PCTFULL ED 20020822

TITLE (ENGLISH): 207 HUMAN SECRETED PROTEINS

TITLE (FRENCH): 207 PROTEINES HUMAINES SECRETEES

INVENTOR(S): NI, Jian;  
EBNER, Reinhard;

LAFLEUR, David, W.;  
 MOORE, Paul, A.;  
 OLSEN, Henrik, S.;  
 ROSEN, Craig, A.;  
 RUBEN, Steven, M.;  
 SOPPET, Daniel, R.;  
 YOUNG, Paul, E.;  
 SHI, Yanggu;  
 FLORENCE, Kimberly, A.;  
 WEI, Ying-Fei;  
 FLORENCE, Charles;  
 HU, Jing-Shan;  
 LI, Yi;  
 KYAW, Hla;  
 FISCHER, Carrie, L.;  
 FERRIE, Ann, M.;  
 FAN, Ping;  
 FENG, Ping;  
 ENDRESS, Gregory, A.;  
 DILLON, Patrick, J.;  
 CARTER, Kennith, C.;  
 BREWER, Laurie, A.;  
 YU, Guo-Liang;  
 ZENG, Zhizhen;  
 GREENE, John, M.

PATENT ASSIGNEE(S):

HUMAN GENOME SCIENCES, INC.;  
 NI, Jian;  
 EBNER, Reinhard;  
 LAFLEUR, David, W.;  
 MOORE, Paul, A.;  
 OLSEN, Henrik, S.;  
 ROSEN, Craig, A.;  
 RUBEN, Steven, M.;  
 SOPPET, Daniel, R.;  
 YOUNG, Paul, E.;  
 SHI, Yanggu;  
 FLORENCE, Kimberly, A.;  
 WEI, Ying-Fei;  
 FLORENCE, Charles;  
 HU, Jing-Shan;  
 LI, Yi;  
 KYAW, Hla;  
 FISCHER, Carrie, L.;  
 FERRIE, Ann, M.;  
 FAN, Ping;  
 FENG, Ping;  
 ENDRESS, Gregory, A.;  
 DILLON, Patrick, J.;  
 CARTER, Kennith, C.;  
 BREWER, Laurie, A.;  
 YU, Guo-Liang;  
 ZENG, Zhizhen;  
 GREENE, John, M.

DOCUMENT TYPE:

Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001062891	A2	20010830

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
 TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
 CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2001-US5614 A 20010221

PRIORITY INFO.:

US 2000-60/184,836 20000224  
 US 2000-60/193,170 20000329

ABEN The present invention relates to the novel human secreted proteins and

isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human secreted proteins. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating diseases, disorders, and/or conditions related to these novel human secreted proteins.

ABFR La presente invention concerne de nouvelles proteines humaines secretees ainsi que des acides nucleiques isoles contenant les regions codantes des genes codant ces proteines. L'invention concerne egalement des vecteurs, des cellules hotes, des anticorps ainsi que des methodes de recombinaison permettant la production de proteines humaines secretees. L'invention concerne egalement des methodes de diagnostic et therapeutiques utiles pour diagnostiquer et traiter des maladies, des troubles et/ou des etats lies a ces nouvelles proteines humaines secretees.

L33 ANSWER 19 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2001057191 PCTFULL ED 20020827  
 TITLE (ENGLISH): GENERATION OF DOPAMINERGIC NEURONS FROM HUMAN NERVOUS SYSTEM STEM CELLS  
 TITLE (FRENCH): PRODUCTION DE NEURONES DOPAMINERGIQUES A PARTIR DE CELLULES SOUCHES DU SYSTEME NERVEUX HUMAIN  
 INVENTOR(S): ZOBEL, Rita;  
 LEVESQUE, Michel, F.  
 PATENT ASSIGNEE(S): NEUROGENERATION, INC.  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001057191	A1	20010809

# DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM  
 HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU  
 LV MA MD MG MN MW MX MZ NO NZ PL PT RO RU SD SE SG  
 SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW GH GM  
 KE LS MW MZ SD SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ  
 TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT  
 SE TR BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US1564 A 20010116  
 PRIORITY INFO.: US 2000-09/490,569 20000201

ABEN The present invention relates to methods for generating dopaminergic neurons in vitro from embryonic and adult central nervous system cells. Specifically, these cells are isolated, cultured in vitro and stimulated to differentiate into dopaminergic neurons by down-regulating COUP-TFI and/or COUP-TFII expression or increasing NOT1 expression. These newly generated dopaminergic neurons may serve as an excellent source for cell replacement therapy in neurological disorders in which the dopaminergic system is compromised.

ABFR Methodes permettant de produire des neurones dopaminergiques in vitro a partir de cellules souches du systeme nerveux central adulte et embryonnaire. Specifiquement, ces cellules sont isolees, cultivees in vitro et stimulees pour se differencier en neurones dopaminergiques par regulation a la baisse de l'expression de COUP-TFI et/ou de COUP-TFII ou par augmentation de l'expression de NOT1. Ces neurones dopaminergiques nouvellement produits peuvent constituer une excellente source pour la therapie de remplacement cellulaire dans des troubles neurologiques dans lesquels le systeme dopaminergique est atteint.

L33 ANSWER 20 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2001053331 PCTFULL ED 20020827  
 TITLE (ENGLISH): PEPTIDOMIMETIC MODULATORS OF CELL ADHESION  
 TITLE (FRENCH): MODULATEURS PEPTIDOMIMETIQUES DE L'ADHESION CELLULAIRE  
 INVENTOR(S): GOUR, Barbara, J.;  
 BLASCHUK, Orest, W.;  
 ALI, Anmar;  
 NI, Feng;  
 CHEN, Zhigang;  
 MICHAUD, Stephanie, Denise;  
 WANG, Shoameng;  
 HU, Zengjian

PATENT ASSIGNEE(S): ADHEREX TECHNOLOGIES, INC.;  
GOUR, Barbara, J.;  
BLASCHUK, Orest, W.;  
ALI, Anmar;  
NI, Feng;  
CHEN, Zhigang;  
MICHAUD, Stephanie, Denise;  
WANG, Shoameng;  
HU, Zengjian  
Patent

DOCUMENT TYPE:  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001053331	A2	20010726

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2001-US2508 A 20010124  
PRIORITY INFO.: US 2000-09/491,078 20000124

ABEN Peptidomimetics of cyclic peptides, and compositions comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

ABFR L'invention concerne des peptidomimetiques de peptides cycliques ainsi que des compositions contenant ces peptidomimetiques. Les peptidomimetiques ont une structure tridimensionnelle sensiblement similaire a une structure tridimensionnelle d'un peptide cyclique contenant une sequence HAV de reconnaissance d'adhesion cellulaire mediee par cadherine. L'invention concerne egalement des methodes d'utilisation de ces peptidomimetiques pour moduler l'adhesion cellulaire mediee par cadherine dans une variete de contextes.

L33 ANSWER 21 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2001047946 PCTFULL ED 20020827  
TITLE (ENGLISH): GFra1-RET SPECIFIC AGONISTS AND METHODS THEREFOR  
TITLE (FRENCH): AGONISTES SPECIFIQUES POUR GRF\$G(A)1-RET ET PROCEDES CORRESPONDANTS  
INVENTOR(S): MILBRANDT, Jeffrey, D.;  
BALOH, Robert, H.  
PATENT ASSIGNEE(S): WASHINGTON UNIVERSITY;  
MILBRANDT, Jeffrey, D.;  
BALOH, Robert, H.  
DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001047946	A2	20010705

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US34852 A 20001221  
PRIORITY INFO.: US 1999-09/473,551 19991228

ABEN Chimeric GDNF family ligands which activate a GFra/RET are disclosed. Included are chimeras which activate GFra1/RET but do not activate GFra2-RET or GFra3-RET. The chimeras are useful in providing trophic support to a mammalian cell or in producing differentiation of a



mammalian cell, or both, particularly when the cell is in a patient suffering from various diseases, in particular Parkinson's Disease.

ABFR L'invention concerne des ligands chimeres de la famille GDNF activant un GFRA/RET. Elle englobe des chimeres activant GRF $\alpha$ 1/RET mais n'activant pas GFRA2-RET ou GRF $\alpha$ 3-RET. Ces chimeres sont utiles pour apporter un support trophique a une cellule mammifere ou pour produire une differenciation de cellules mammiferes, ou les deux, en particulier quand la cellule appartient a un patient atteint de differentes maladies, en particulier, la maladie de Parkinson.

L33 ANSWER 22 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2001042451 PCTFULL ED 20020827  
 TITLE (ENGLISH): FULL-LENGTH HUMAN cDNAs ENCODING POTENTIALLY SECRETED PROTEINS  
 TITLE (FRENCH): ADnc HUMAINS PLEINE LONGUEUR CODANT POUR DES PROTEINES POTENTIELLEMENT SECRETEES  
 INVENTOR(S): DUMAS MILNE EDWARDS, Jean-Baptiste;  
 BOUGUELERET, Lydie;  
 JOBERT, Severin  
 PATENT ASSIGNEE(S): GENSET;  
 DUMAS MILNE EDWARDS, Jean-Baptiste;  
 BOUGUELERET, Lydie;  
 JOBERT, Severin  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001042451	A2	20010614

#### DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
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 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF  
 CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-IB1938 A 20001207  
 PRIORITY INFO.: US 1999-60/169,629 19991208  
 US 2000-60/187,470 20000306

ABEN The invention concerns GENSET polynucleotides and polypeptides. Such GENSET products may be used as reagents in forensic analyses, as chromosome markers, as tissue/cell/organelle-specific markers, in the production of expression vectors. In addition, they may be used in screening and diagnosis assays for abnormal GENSET expression and/or biological activity and for screening compounds that may be used in the treatment of GENSET-related disorders.

ABFR L'invention concerne des polynucleotides et des polypeptides GENSET. Ces produits GENSET peuvent s'utiliser comme reactifs dans des analyses judiciaires, en tant que marqueurs chromosomiques, comme marqueurs specifiques a un tissu/cellule/organite, dans la production de vecteurs d'expression. En outre, ils peuvent s'utiliser dans des dosages de criblage et diagnostiques d'une expression GENSET et/ou une activite biologique anormales ainsi que pour le criblage de composees pouvant etre utilisees dans le traitement de troubles lies a GENSET.

L33 ANSWER 23 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2001030981 PCTFULL ED 20020820  
 TITLE (ENGLISH): CULTURES OF GFAP?+&quest; NESTIN?+&quest; CELLS THAT DIFFERENTIATE TO NEURONS  
 TITLE (FRENCH): CULTURES DE CELLULES GFAP?+&quest; NESTIN?+&quest; SE DIFFERENCIANT EN NEURONES  
 INVENTOR(S): WAHLBERG, Lars;  
 CAMPBELL, Kenneth;  
 FAGERSTROM, Charlotta;  
 ERIKSSON, Cecilia;  
 WICTORIN, Klas  
 PATENT ASSIGNEE(S): NS GENE A/S;  
 WAHLBERG, Lars;  
 CAMPBELL, Kenneth;  
 FAGERSTROM, Charlotta;

DOCUMENT TYPE:  
PATENT INFORMATION:

ERIKSSON, Cecilia;  
WICTORIN, Klas  
Patent

NUMBER	KIND	DATE
WO 2001030981	A1	20010503

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG  
CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:  
PRIORITY INFO.:

WO 2000-IB1669	A	20001025
US 1999-60/161,316		19991025
US 2000-60/161,316		20001024

ABEN Cultures of cells immunoreactive for glial fibrillary acidic protein (GFAP), as well as for the intermediate filament marker nestin were grown in a medium including epidermal growth factor (EGF) and serum. The cultured cells had the morphology of astroglial cells. The cells can be proliferated in adherent or suspension cultures. Depending on the culture conditions, the cells can be induced to differentiate to neurons or glial cells. The cultures can be expanded over a large number of passages during several months, and survive, express an astroglial phenotype and integrate well after transplantation into both neonatal and adult rat forebrain.

ABFR

L33 ANSWER 24 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 2001022978 PCTFULL ED 20020820  
TITLE (ENGLISH): AUTOLOGOUS MARROW STEM CELL (MSC) TRANSPLANTATION FOR MYOCARDIAL REGENERATION  
TITLE (FRENCH): TRANSPLANTATION DE CELLULES SOUCHES (MSC) DE MOELLE OSSEUSE AUTOLOGUES EN VUE DE LA REGENERATION MYOCARDIQUE  
INVENTOR(S): CHIU, Ray, C., J.;  
SHUM-TIM, Dominique;  
GALIPEAU, Jacques  
PATENT ASSIGNEE(S): MCGILL UNIVERSITY;  
CHIU, Ray, C., J.;  
SHUM-TIM, Dominique;  
GALIPEAU, Jacques  
DOCUMENT TYPE:  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001022978	A2	20010405

DESIGNATED STATES  
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU  
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN  
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK  
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD  
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY  
DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG  
CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:  
PRIORITY INFO.:

WO 2000-CA1114	A	20000928
US 1999-60/156,700		19990930

ABEN The present invention relates to a method of improving cardiac function in a patient with heart failure without eliciting an immune response and without sacrificing the patient's skeletal muscle; which comprises the step of transplanting autologous bone marrow stroma cells (MSCs) into said patient's myocardium to grow new muscle fibers. The method may further comprise the step of using cell labeling technique to confirm survival and differentiation of implanted MSCs, and to identify said MSCs phenotype by both morphology and molecular markers. The method may further comprise examining the effects of the micro-environment of implanted MSCs on their differentiation and phenotype expression. The

method may further comprise examining functional contribution of MSCs implanted into an ischemic segment of the myocardium.

ABFR

L33 ANSWER 25 OF 63 USPATFULL on STN

ACCESSION NUMBER: 2001:126193 USPATFULL  
TITLE: Cells and methods for the generation of transgenic pigs  
INVENTOR(S): Piedrahita, Jorge A., College Station, TX, United States  
Bazer, Fuller W., College Station, TX, United States  
PATENT ASSIGNEE(S): The Texas A & M University System, College Station, TX, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6271436	B1	20010807
APPLICATION INFO.:	US 1997-949155		19971010 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-27338P	19961011 (60)
	US 1997-46094P	19970509 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Martin, Jill D.	
LEGAL REPRESENTATIVE:	Williams, Morgan & Amerson	
NUMBER OF CLAIMS:	69	
EXEMPLARY CLAIM:	55	
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)	
LINE COUNT:	8905	

AB Disclosed are methods for the isolation of primordial germ cells, culturing these cells to produce primordial germ cell-derived cell lines, methods for transforming both the primordial germ cells and the cultured cell lines, and using these transformed cells and cell lines to generate transgenic animals. The efficiency at which transgenic animals are generated by the present invention is greatly increased, thereby allowing the use of homologous recombination in producing transgenic non-rodent animal species.

L33 ANSWER 26 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 2000018799 PCTFULL ED 20020515  
TITLE (ENGLISH): ARTEMIN, A NOVEL NEUROTROPHIC FACTOR  
TITLE (FRENCH): L'ARTEMINE, UN NOUVEAU FACTEUR NEUROTROPHIQUE  
INVENTOR(S): MILBRANDT, Jeffrey, D.;  
BALOH, Robert, H.  
PATENT ASSIGNEE(S): WASHINGTON UNIVERSITY;  
MILBRANDT, Jeffrey, D.;  
BALOH, Robert, H.

LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent

	NUMBER	KIND	DATE
PATENT INFORMATION:	WO 2000018799	A1	20000406

DESIGNATED STATES

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE  
DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE  
KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO  
NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US  
UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG ZW AM AZ  
BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR  
IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR  
NE SN TD TG

APPLICATION INFO.:	WO 1999-US22604	A	19990929
PRIORITY INFO.:	US 1998-09/163,283		19980929
	US 1998-60/108,148		19981112
	US 1998-09/218,698		19981222

ABEN A novel growth factor, artemin, which belongs to the GDNF/neurturin/persephin family of growth factors, is disclosed. The human and mouse amino sequences have been

identified. Human and mouse artemin genomic DNA sequences have been cloned and sequenced and the respective cDNA sequences identified. In addition, methods for treating degenerative conditions using artemin, methods for detecting artemin gene alterations and methods for detecting and monitoring patient levels of artemin are provided.

ABFR L'invention concerne un nouveau facteur de croissance, l'artemine, qui appartient a la famille des facteurs de croissance GDNF/neurturine/persephine. Les sequences amino humaines et murines ont ete identifiees. Les sequences de l'ADN genomique de l'artemine humaine et murine ont ete clonees et sequencees, et l'on a identifie les sequences d'ADNc respectives. L'invention concerne egalement des procedes relatifs au traitement des etats degeneratifs par le biais de l'artemine, ainsi que des procedes relatifs a la detection des alterations du gene de l'artemine et des procedes relatifs a la detection et au controle des niveaux d'artemine chez les patients.

L33 ANSWER 27 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 2000002917 PCTFULL ED 20020515  
 TITLE (ENGLISH): COMPOUNDS AND METHODS FOR MODULATING CADHERIN-MEDIATED FUNCTIONS  
 TITLE (FRENCH): COMPOSES PERMETTANT DE MODULER DES FONCTIONS INDUITES PAR LA CADHERINE ET TECHNIQUES AFFERENTES  
 INVENTOR(S): DOHERTY, Patrick;  
 BLASCHUK, Orest, W.;  
 GOUR, Barbara, J.  
 PATENT ASSIGNEE(S): ADHEREX TECHNOLOGIES, INC.;  
 DOHERTY, Patrick;  
 BLASCHUK, Orest, W.;  
 GOUR, Barbara, J.  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2000002917	A2	20000120

# DESIGNATED STATES

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP  
 KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL  
 PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN  
 YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ  
 MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU  
 MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD  
 TG

APPLICATION INFO.: WO 1999-CA627 A 19990712  
 PRIORITY INFO.: US 1998-09/113,977 19980710

ABEN Modulating agents and methods for enhancing or inhibiting cadherin-mediated functions are provided. The modulating agents comprise at least an HAV binding motif, an analogue or peptidomimetic thereof, or an antibody or fragment thereof that specifically binds to such a motif. Modulating agents may additionally comprise one or more cell adhesion recognition sequences recognized by cadherins and/or other adhesion molecules. Such modulating agents may, but need not, be linked to a targeting agent, drug and/or support material.

ABFR Cette invention a trait a des agents de modulation et aux techniques afferentes renforçant ou inhibant des fonctions lies a la cadherine. Ces agents de modulation comportent au moins un motif de reconnaissance d'adhesion a HAV (His-Ala-Val), un analogue ou un peptidomimetique de celui-ci ou un anticorps ou un fragment de celui-ci se liant de maniere specifique a ce motif. Les agents de

modulation peuvent, de surcroit, comporter une ou plusieurs sequences de reconnaissance d'adhesion cellulaire reconnues par des cadherines et/ou d'autres molecules d'adhesion. Ils peuvent, sans pour autant y etre contraints, etre lies a un agent de ciblage, a un medicament et/ou a un materiau support.

L33 ANSWER 28 OF 63 USPATFULL on STN

ACCESSION NUMBER: 2000:105411 USPATFULL  
 TITLE: Genetically engineered cells that produce produce L. Dopa  
 INVENTOR(S): Kang, Un Jung, Northbrook, IL, United States  
 Gage, Fred H., La Jolla, CA, United States  
 PATENT ASSIGNEE(S): Arch Development Corporation, Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6103226		20000815
APPLICATION INFO.:	US 1994-290028		19940812 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	LeGuyader, John I.		
ASSISTANT EXAMINER:	McGarry, Sean		
LEGAL REPRESENTATIVE:	Rockey, Milnamow & Katz, Ltd.		
NUMBER OF CLAIMS:	25		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 1 Drawing Page(s)		
LINE COUNT:	1247		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a process of increasing dopamine production in a cell comprising co-transfecting the cell with one or more expression vectors containing polynucleotides that encode tyrosine hydroxylase, aromatic L-amino acid decarboxylase and GTP cyclohydrolase. Cells transfected with such vectors and the use of such transformed cells to increase dopamine production in the central nervous system of animals are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L33 ANSWER 29 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
 on STN DUPLICATE 2

ACCESSION NUMBER: 2000271026 EMBASE  
 TITLE: [Neural transplants in Parkinson's disease: Clinical results after 10 years' experience].  
 TRASPLANTES NEURALES EN LA ENFERMEDAD DE PARKINSON:  
 RESULTADOS CLINICOS TRAS 10 ANOS DE EXPERIENCIA.  
 AUTHOR: Lopez-Lozano J.J.; Mata M.; Bravo G.  
 CORPORATE SOURCE: Dr. J.J. Lopez-Lozano, Unidad Trasplan. Neur. Restr. Nerv.,  
 Clinica Puerta de Hierro, San Martin de Porres, 4, E-28035  
 Madrid, Spain. jlozano@cexp.cph.es  
 SOURCE: Revista de Neurologia, (1 Jun 2000) 30/11 (1077-1083).  
 Refs: 81  
 ISSN: 0210-0010 CODEN: RVNRAA  
 COUNTRY: Spain  
 DOCUMENT TYPE: Journal; Conference Article  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 LANGUAGE: Spanish  
 SUMMARY LANGUAGE: English; Spanish; Italian

AB Introduction. At the end of the 1970s people considered the possibility that transplants might be useful to replace degenerate specific cell populations, such as the mesencephalic dopaminergic neurones in Parkinson's disease (PD). Since then this has become an experimental alternative treatment for patients with degenerative diseases. The history of transplants of catecholamine producing tissues within the brain of patients with PD started in 1985, when Backlund et al published the results of the first implants of autologous adrenal medulla in two patients with Parkinsonism. Since then, many patients throughout the world have benefited from the results obtained using this method. Two main types of tissue have been used in this

method.' autologous adrenal medulla and human foetal ventral mesencephalic tissue. Development. In this paper we first review the clinical effects of the diverse types of transplant done to date. Then in the second part we give a summary of the clinical results obtained by our group with the different types of transplant carried out. We explain their evolution, original hypothesis and justify the reasons which led us to use three different types of donor material: autologous adrenal medulla, fetal tissue and adrenal medulla co-incubated with peripheral nerve. Then, after showing that the clinical improvement is different depending on the type of tissue **transplanted**, we comment on the probable reason for the improvement seen in patients with implants. Conclusion. The **transplantation** of nervous tissue seems to us to be no longer an experimental alternative for the treatment of PD but has become an effective, lasting treatment for patients with Parkinson's disease.

L33 ANSWER 30 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 1999057149 PCTFULL ED 20020515  
 TITLE (ENGLISH): COMPOUNDS AND METHODS FOR MODULATING NONCLASSICAL  
 CADHERIN-MEDIATED FUNCTIONS  
 TITLE (FRENCH): COMPOSES ET PROCEDES SERVANT A MODULER DES FONCTIONS  
 ETABLIES PAR L'INTERMEDIAIRE DE CADHERINE NON CLASSIQUE  
 INVENTOR(S): BLASCHUK, Orest, W.;  
 GOUR, Barbara, J.;  
 BYERS, Stephen  
 PATENT ASSIGNEE(S): ADHEREX TECHNOLOGIES, INC.;  
 BLASCHUK, Orest, W.;  
 GOUR, Barbara, J.;  
 BYERS, Stephen  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9957149	A2	19991111

DESIGNATED STATES  
 W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP  
 KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL  
 PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN  
 YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ  
 MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU  
 MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD  
 TG

APPLICATION INFO.: WO 1999-CA363 A 19990505  
 PRIORITY INFO.: US 1998-09/073,040 19980505  
 US 1998-09/187,859 19981106  
 US 1999-09/234,395 19990120  
 US 1999-09/264,516 19990308

ABEN Modulating agents for inhibiting or enhancing nonclassical cadherin mediated cell adhesion are provided. The modulating agents comprise one or more of: (a) a peptide sequence that is at least 50 % identical to a nonclassical cadherin CAR sequence; (b) a non-peptide mimetic of a nonclassical cadherin CAR sequence; (c) a substance, such as an antibody or antigen-binding fragment thereof, that specifically binds a nonclassical cadherin CAR sequence; and/or (d) a polynucleotide encoding a polypeptide that comprises a nonclassical cadherin CAR sequence or analogue thereof. Methods for using such modulating agents for modulating nonclassical cadherin-mediated cell adhesion in a variety of contexts are also provided.

ABFR L'invention concerne des agents de modulation servant a inhiber ou a amplifier l'adhesion cellulaire creee par l'intermediaire de cadherine non classique. Ces agents de modulation comprennent un ou plusieurs elements parmi (a) une sequence de peptides au moins identique a 50 % a une sequence CAR de cadherine non classique; (b) un mimetique non

peptidique d'une sequence CAR de  
cadherine non classique; (c) une substance, telle qu'un anticorps ou un  
de ses fragments de liaison  
a un antigene, se fixant de facon specifique a une sequence CAR de  
cadherine non classique et/ou (d)  
un polynucleotide codant un polypeptide contenant une sequence CAR de  
cadherine non classique ou un  
de ses analogues. Elle concerne egalement des procedes servant a  
utiliser ces agents de modulation  
afin de moduler l'adhesion cellulaire creee par l'intermediaire de  
cadherine non classique dans une  
variete de contextes.

L33 ANSWER 31 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1999016791 PCTFULL ED 20020515  
TITLE (ENGLISH): COMPOUNDS AND METHODS FOR REGULATING CELL ADHESION  
TITLE (FRENCH): COMPOSES ET PROCEDES DE REGULATION D'ADHERENCE  
CELLULAIRE  
INVENTOR(S): BLASCHUCK, Orest, W.;  
GOUR, Barbara, J.  
PATENT ASSIGNEE(S): ADHEREX INC.;  
BLASCHUCK, Orest, W.;  
GOUR, Barbara, J.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9916791	A2	19990408

# DESIGNATED STATES

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC  
LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH  
GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT  
BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF  
BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-CA902 A 19980929  
PRIORITY INFO.: US 1997-08/939,853 19970929

ABEN Methods for using modulating agents to enhance or inhibit  
cadherin-mediated cell adhesion in a  
variety of i(in vivo) and i(in vitro) contexts are provided. In  
particular, the modulating agents  
may be used in the therapy of multiple sclerosis and other demyelinating  
diseases. The modulating  
agents comprise at least one cadherin cell adhesion recognition sequence  
(HAV) or an antibody or  
fragment thereof that specifically binds to a cadherin cell adhesion  
recognition sequence.  
Modulating agents may additionally comprise one or more cell adhesion  
recognition sequences  
recognized by other adhesion molecules. Such modulating agents may, but  
need not, be linked to a  
targeting agent, drug and/or support material.

ABFR L'invention concerne des procedes d'utilisation d'agents de modulation  
permettant d'ameliorer  
ou d'inhiber l'adherence cellulaire a mediation de cadherine dans une  
variete de contextes i(in vivo  
)et i(in vitro. )Plus particulierement, les agents de modulation peuvent  
etre utilises dans la  
therapie de la sclerose en plaques et d'autres maladies demyelinisantes.  
Lesdits agents comportent  
au moins une sequence de reconnaissance d'adherence cellulaire a  
mediation de cadherine (HAV) ou un  
anticorps ou fragment d'anticorps qui se lie specifiquement a une  
sequence de reconnaissance  
d'adherence cellulaire a mediation de cadherine. Les agents de  
modulation peuvent comprendre en  
outre une ou plusieurs sequences de reconnaissance d'adherence  
cellulaire a mediation de cadherine  
reconnues par d'autres molecules d'adherence. De tels agents de

modulation peuvent, sans pour autant  
y etre contraints, etre lies a un agent de ciblage, un medicament et/ou  
un materiau support.

L33 ANSWER 32 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1999014235 PCTFULL ED 20020515  
TITLE (ENGLISH): PERSEPHIN AND RELATED GROWTH FACTORS  
TITLE (FRENCH): PERSEPHINE ET FACTEURS DE CROISSANCE ASSOCIES  
INVENTOR(S): JOHNSON, Eugene, M.;  
MILBRANDT, Jeffrey, D.;  
KOTZBAUER, Paul, T.;  
LAMPE, Patricia, A.;  
KLEIN, Robert;  
DeSAUVAGE, Fred  
PATENT ASSIGNEE(S): WASHINGTON UNIVERSITY;  
JOHNSON, Eugene, M.;  
MILBRANDT, Jeffrey, D.;  
KOTZBAUER, Paul, T.;  
LAMPE, Patricia, A.;  
KLEIN, Robert;  
DeSAUVAGE, Fred  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9914235	A1	19990325

DESIGNATED STATES

W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC  
LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH  
GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT  
BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF  
BJ CF CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-US19163 A 19980915  
PRIORITY INFO.: US 1997-08/931,858 19970916

ABEN A novel growth factor, persephin, which belongs to the GDNF/neurturin family of growth factors, is disclosed. The human, mouse and rat amino acid sequences have been identified. Human, mouse and rat persephin genomic DNA sequences have been cloned and sequenced and the respective cDNA sequences identified. In addition, methods for treating degenerative conditions using persephin, methods for detecting persephin gene alterations and methods for detecting and monitoring patient levels of persephin are provided. Methods for identifying additional members of the persephin-neurturin-GDNF family of growth factors are also provided.

ABFR L'invention se rapporte a un nouveau facteur de croissance, la persephine, qui fait partie de la famille GDNF/neurturine des facteurs de croissance. On a identifie des sequences d'acides amines de l'humain, du rat et de la souris. Les sequences d'ADN genomique de la persephine chez l'humain, le rat et la souris ont ete clonees et mises en sequences, et l'on a identifie les sequences de l'ADN-c correspondants. En outre, l'invention se rapporte a des procedes pour traiter a la persephine les etats de degenerescence, a des procedes pour detecter les alterations du gene de la persephine et a des procedes pour detecter et surveiller le taux de persephine des patients. L'invention concerne egalement des procedes pour identifier d'autres membres de la famille de la persephine-neurturine-GDNF des facteurs de croissance.

L33 ANSWER 33 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 3  
ACCESSION NUMBER: 1999315130 EMBASE



TITLE: Isolation and intracerebral grafting of nontransformed multipotential embryonic human CNS stem cells.  
 AUTHOR: Vescovi A.L.; Gritti A.; Galli R.; Parati E.A.  
 CORPORATE SOURCE: Dr. A.L. Vescovi, Natl. Neurol. Institute 'C. Besta', Via Celoria 11, 20133 Milan, Italy. vescovi@tin.it  
 SOURCE: Journal of Neurotrauma, (1999) 16/8 (689-693).  
 Refs: 15  
 ISSN: 0897-7151 CODEN: JNEUE4  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Conference Article  
 FILE SEGMENT: 008 Neurology and Neurosurgery  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB In this work, we show that the embryonic human brain contains multipotent central nervous system (CNS) stem cells, which may provide a continuous, standardized source of human neurons that could virtually eliminate the use of primary human fetal brain tissue for intracerebral **transplantation**. Multipotential stem cells can be isolated from the developing human CNS in a reproducible fashion and can be exponentially expanded for longer than 2 years. This allows for the establishment of continuous, nontransformed neural cell lines, which can be frozen and banked. By clonal analysis, reverse transcription polymerase chain reaction, and electrophysiological assay, we found that over **such** long-term culturing these cells retain both multipotentiality and an unchanged capacity for the generation of neuronal cells, and that they can be induced to differentiate into catecholaminergic neurons. Finally, when transplanted into the brain of adult rodents immunosuppressed by cyclosporin A, human CNS stem cells migrate away from the site of injection and differentiate into neurons and astrocytes. No tumor formation was ever observed. Aside from depending on scarce human neural fetal tissue, the use of human embryonic CNS stem cells for clinical neural **transplantation** should provide a reliable solution to some of the major problems that pertain to this field, and should allow determination of the safety characteristics of the **donor** cells in terms of tumorigenicity, viability, sterility, and antigenic compatibility far in advance of the scheduled day of surgery.

L33 ANSWER 34 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 1998045319 PCTFULL ED 20020514  
 TITLE (ENGLISH): COMPOUNDS AND METHODS FOR INHIBITING THE INTERACTION BETWEEN 'alpha'-CATENIN and 'beta'-CATENIN  
 TITLE (FRENCH): COMPOSES ET PROCEDES PERMETTANT D'INHIBER L'INTERACTION ENTRE L''alpha'-CATENINE ET LA 'beta'-CATENINE  
 INVENTOR(S): BLASCHUK, Orest, W.;  
 GOUR, Barbara, J.  
 PATENT ASSIGNEE(S): MCGILL UNIVERSITY;  
 BLASCHUK, Orest, W.;  
 GOUR, Barbara, J.  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9845319	A2	19981015

DESIGNATED STATES  
 W:

AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
 ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC  
 LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU  
 SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH  
 GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT  
 BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF  
 BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-CA322 A 19980414  
 PRIORITY INFO.: US 1997-60/043,361 19970410

ABEN Modulating agents for inhibiting an interaction between 'alpha'-catenin and 'beta'-catenin are provided. The modulating agents comprise one or more of: (a) a 'beta'-catenin HAV motif; (b) a peptide analogue or mimetic of a 'beta'-catenin HAV motif; or (c) an antibody or antigen-binding fragment thereof that specifically binds to a 'beta'-catenin HAV motif.

Methods for using such modulating agents for inhibiting cadherin-mediated cell adhesion in a variety of contexts are also provided.

ABFR L'invention concerne des agents modulateurs permettant d'inhiber une interaction entre l''alpha'-catenine et la 'beta'-catenine. Ces agents modulateurs contiennent (a) un ou plusieurs motifs HAV de la 'beta'-catenine; (b) un ou plusieurs analogues peptidiques ou composes peptidomimetiques du motif HAV d'une 'beta'-catenine; ou (c) un ou plusieurs anticorps ou fragments de fixation de l'antigene de ce motif qui se fixent en particulier sur un motif HAV de la 'beta'-catenine. L'invention se rapporte egalement a des procedes d'utilisation de ces agents modulateurs, procedes visant a inhiber l'adherence intercellulaire due a la cadherine, et ce, dans une pluralite de contextes.

L33 ANSWER 35 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1998016630 PCTFULL ED 20020514  
TITLE (ENGLISH): METHODS FOR THE GENERATION OF PRIMORDIAL GERM CELLS AND TRANSGENIC ANIMAL SPECIES  
TITLE (FRENCH): TECHNIQUES PERMETTANT LA PRODUCTION DE CELLULES SEXUELLES PRIMORDIALES ET D'ESPECES ANIMALES TRANSGENIQUES  
INVENTOR(S): PIEDRAHITA, Jorge, A.;  
BAZER, Fuller, W.  
PATENT ASSIGNEE(S): THE TEXAS A & M UNIVERSITY SYSTEM;  
PIEDRAHITA, Jorge, A.;  
BAZER, Fuller, W.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9816630	A1	19980423

DESIGNATED STATES

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE  
ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS  
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG  
SI SK SL TJ TM TR TT UA UG US US UZ VN YU ZW GH KE LS  
MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE  
DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI  
CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US18644 A 19971010  
PRIORITY INFO.: US 1996-60/027,338 19961011  
US 1997-60/046,094 19970509

ABEN Disclosed are methods for the isolation of primordial germ cells, culturing these cells to produce primordial germ cell-derived cell lines, methods for transforming both the primordial germ cells and the cultured cell lines, and using these transformed cells and cell lines to generate transgenic animals. The efficiency at which transgenic animals are generated by the present invention is greatly increased, thereby allowing the use of homologous recombination in producing transgenic non-rodent animal species.

ABFR L'invention, qui a trait a des techniques d'isolation de cellules sexuelles primordiales et de culture de ces cellules aux fins de la production de lignees cellulaires derivees de la cellule sexuelle primordiale, porte egalement sur des techniques de transformation, tant des cellules sexuelles primordiales que des lignees cellulaires derivees, ainsi que sur des techniques d'utilisation de ces cellules transformees et des lignees cellulaires aux fins de la production d'animaux transgeniques. Cette invention, qui permet d'ameliorer

notablement le rendement de cette  
production d'animaux transgeniques, autorise l'emploi de processus de  
recombinaison homologue dans  
la production d'especes animales transgeniques, a savoir des  
non-rongeurs.

L33 ANSWER 36 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1997033911 PCTFULL ED 20020514  
TITLE (ENGLISH): PERSEPHIN AND RELATED GROWTH FACTORS  
TITLE (FRENCH): PERSEPHINE ET FACTEURS DE CROISSANCE ASSOCIES  
INVENTOR(S): JOHNSON, Eugene, M., Jr.;  
MILBRANDT, Jeffrey, D.;  
KOTZBAUER, Paul, T.;  
LAMPE, Patricia, A.  
PATENT ASSIGNEE(S): WASHINGTON UNIVERSITY;  
JOHNSON, Eugene, M., Jr.;  
MILBRANDT, Jeffrey, D.;  
KOTZBAUER, Paul, T.;  
LAMPE, Patricia, A.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9733911	A1	19970918

DESIGNATED STATES  
W:

AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES  
FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV  
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ  
TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ  
BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE  
IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN  
TD TG

APPLICATION INFO.: WO 1997-US3461 A 19970314  
PRIORITY INFO.: US 1996-8/615,944 19960314

ABEN A novel growth factor, persephin, which belongs to the GDNF/neurturin family of growth factors, is disclosed. The mouse and rat amino acid sequences have been identified. Mouse and rat persephin genomic DNA sequences have been cloned and sequenced and the respective cDNA sequences identified. In addition, methods for treating degenerative conditions using persephin, methods for detecting persephin gene alterations and methods for detecting and monitoring patient levels of persephin are provided. Methods for identifying additional members of the persephin-neurturin-GDNF family of growth factors are also provided.

ABFR L'invention concerne un nouveau facteur de croissance, la persephine, qui appartient a la famille de la neurturine/GDNF des facteurs de croissance. Les sequences d'acides amines du rat et de la souris ont ete identifiees. Les sequences d'ADN genomique de la persephine du rat et de la souris ont ete clonees et mises en sequences, et les sequences d'ADNc respectives identifiees. En outre, l'invention a pour objet des procedes pour traiter les etats de degenerescence a l'aide de la persephine, des procedes pour detecter les alterations du gene de la persephine, et des procedes pour detecter et controler les taux de persephine des patients. L'invention traite aussi de procedes pour identifier les membres supplementaires de la famille de la persephine-neurturine-GDNF des facteurs de croissance.

L33 ANSWER 37 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1997024924 PCTFULL ED 20020514  
TITLE (ENGLISH): THE PRESERVATION OF TISSUE DURING REMOVAL, STORAGE AND IMPLANTATION  
TITLE (FRENCH): PRESERVATION DE TISSUS PENDANT LEUR PRELEVEMENT, LEUR

INVENTOR(S): STOCKAGE ET LEUR IMPLANTATION  
 SIMPKINS, James, W.;  
 GREEN, Pattie, S.;  
 GRIDLEY, Kelly, E.  
 PATENT ASSIGNEE(S): UNIVERSITY OF FLORIDA RESEARCH FOUNDATION, INC.  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9724924	A1	19970717

DESIGNATED STATES

W: AU CA JP KR AT BE CH DE DK ES FI FR GB GR IE IT LU MC  
 NL PT SE

APPLICATION INFO.: WO 1997-US482 A 19970110  
 PRIORITY INFO.: US 1996-60/009,705 19960111  
 US 1996-8/685,574 19960724

ABEN The present invention is directed to a method for enhancing cell viability in a population of graft cells during a transplantation procedure that includes the steps of selecting an effective dose of a polycyclic phenolic compound in a physiological acceptable formulation, exposing the population of graft cells to the formulation containing the compound within a time that is effectively proximate to the transplantation procedure, and conferring cytoprotection on the population of graft cells. The polycyclic compound may include a four ring, a three ring, or a two ring structure, having a molecular weight of less than 1000 Daltons. The compound may have a molecular weight of greater than 170 Daltons. The effective dose of the compound may achieve concentrations less than 200nM or greater than 0.2nM. The method may further comprise the step of exposing the graft cells to the compound prior to removal from the donor, during storage in vitro or during reperfusion in the recipient animal.

ABFR L'invention porte sur une methode accroissant la viabilite d'une population de cellules greffees lors d'une transplantation. Ladite methode consiste a selectionner une dose efficace d'un compose phenolique polycyclique place dans une preparation a compatibilite physiologique et a exposer cette population de cellules a ladite preparation pendant un temps correspondant au processus de transplantation, de maniere a conferer une cyto-protection a la population de cellules greffees. Le compose polycyclique peut presenter une structure a quatre, trois ou deux cycles d'un poids moleculaire inferieur a 1000 daltons et superieur a 170 daltons. La dose efficace du compose peut presenter une concentration comprise entre 200nM et 0,2nM. La methode peut egalement comprendre une etape consistant a exposer les cellules greffees au compose avant leur prelevement sur le donneur, ou pendant leur stockage in vitro ou la reperfusion de l'animal recepateur.

L33 ANSWER 38 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 1997008196 PCTFULL ED 20020514  
 TITLE (ENGLISH): NEURTURIN AND RELATED GROWTH FACTORS  
 TITLE (FRENCH): NEURTURIN ET FACTEURS DE CROISSANCE CONNEXES  
 INVENTOR(S): JOHNSON, Eugene, M., Jr.;  
 MILBRANDT, Jeffrey, D.;  
 KOTZBAUER, Paul, T.;  
 LAMPE, Patricia, A.  
 PATENT ASSIGNEE(S): WASHINGTON UNIVERSITY;  
 JOHNSON, Eugene, M., Jr.;  
 MILBRANDT, Jeffrey, D.;  
 KOTZBAUER, Paul, T.;

LANGUAGE OF PUBL.: LAMPE, Patricia, A.  
DOCUMENT TYPE: English  
PATENT INFORMATION: Patent

NUMBER	KIND	DATE
WO 9708196	A1	19970306

DESIGNATED STATES

W:

AL AM AT AU AZ BB BG BR BY CA CH CN CU CZ DE DK EE ES  
FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV  
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ  
TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG  
KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU  
MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1996-US14065 A 19960827

PRIORITY INFO.: US 1995-8/519,777 19950828

ABEN A novel growth factor, neurturin, is disclosed and the human and mouse amino acid sequences are identified. Human and mouse neurturin genomic DNA sequences have been cloned and sequenced and the respective cDNA sequences identified. The subcloning into vectors and the preparation of cells stably transformed with the vectors are also disclosed. In addition, methods for treating degenerative conditions, tumor cells and obesity; methods for detecting gene alterations and methods for detecting and monitoring patient levels of neurturin are provided. Methods for identifying additional members of the neurturin-GDNF family of growth factors are also provided.

ABFR L'invention porte sur un nouveau facteur de croissance, nomme neurturin, ainsi que sur l'identification des sequences d'acides amines chez l'homme et la souris. On a clone et sequence des sequences d'ADN genomique de neurturin chez l'homme et la souris et identifie les sequences d'ADN complementaire respectives. L'invention, qui porte sur un clonage complementaire en vecteurs ainsi que sur la production de cellules transformees de facon stable par lesdits vecteurs, concerne egalement des methodes de traitement de pathologies degeneratives, de l'obesite et de cellules tumorales, des procedes de detection de modifications de gene ainsi que de detection et de surveillance de taux de neurturin chez un patient et, enfin, des procedes permettant l'identification d'elements complementaires de la famille GDNF-neurturin (facteur neurotrophique derive de la cellule gliale) des facteurs de croissance.

I33 ANSWER 39 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 4

ACCESSION NUMBER: 97026331 EMBASE  
DOCUMENT NUMBER: 1997026331  
TITLE: Discordant xenogeneic neonatal thymic transplantation can induce donor- specific tolerance.  
AUTHOR: Khan A.; Sergio J.J.; Zhao Y.; Pearson D.A.; Sachs D.H.; Sykes M.  
CORPORATE SOURCE: Dr. M. Sykes, Surgical Service, Transplantation Biology Res. Center, Massachusetts General Hospital, 13th Street, Boston, MA 02129, United States  
SOURCE: Transplantation, (1997) 63/1 (124-131).  
Refs: 13  
ISSN: 0041-1337 CODEN: TRPLAU  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The limited supply of human organs for **transplantation** necessitates the development of methods leading to acceptance of

xenografts. To avoid the hazards of the high-dose chronic immunosuppressive pharmacotherapy which would otherwise be required for **successful** xenografting, it would be desirable to induce permanent tolerance to xenogeneic donors. We have recently demonstrated that xenogeneic donor-specific tolerance can be induced by **transplanting** fetal pig thymic and hematopoietic tissue into thymectomized, T cell-depleted, and natural killer-cell-depleted mice, or into natural killer cell-depleted nude mice. We have now extended these studies by replacing fetal tissue with neonatal pig thymic and hematopoietic tissue, and by examining the in vivo responses of reconstituted mice to pig skin grafts. Neonatal tissue was studied because it might be more practicable than **fetal tissue** for the purpose of **transplantation** to primates. BALB/c nu/nu mice **transplanted** with neonatal (<24-hr-old) pig thymus and spleen fragments developed circulating mouse CD4+ cells. The pig thymus grafts were necessary for mouse T-cell development, as CD4 recovery did not occur in recipients of neonatal pig splenic tissue alone. The CD4+ cells that developed included V $\beta$ 8.1/2+ T cells in similar proportions as in BALB/c mice, and V $\beta$ 11+ and V $\beta$ 5+ CD4 T cells were deleted almost as completely as in normal BALB/c mice. This deletion was detected among CD4 single-positive graft thymocytes. In 9 of 12 evaluable animals, mixed lymphocyte responses demonstrated tolerance to **donor-type** pig SLA antigens, with responsiveness to alloantigens and/or third-party pig xenoantigens. Furthermore, grafting of neonatal pig thymus conferred the ability to reject allogeneic mouse skin in 7 of 10 animals. In addition, 7 of 10 animals accepted paternal (**donor** SLA-matched) skin (median survival time [MST] > 100 days), whereas 4 of 4 animals rejected third-party SLA-mismatched pig skin (MST=40.5 days). We conclude that neonatal pig thymi transplanted to BALB/c nu/nu mice can support the development of mouse CD4+ cells that are functional and specifically tolerant to **donor-type** pig antigens.

L33 ANSWER 40 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 1996037208 PCTFULL ED 20020514  
 TITLE (ENGLISH): ALLOGENEIC CELL THERAPY FOR CANCER FOLLOWING ALLOGENEIC  
 STEM CELL TRANSPLANTATION  
 TITLE (FRENCH): THERAPIE CELLULAIRE ALLOGENIQUE ANTICANCEREUSE SUIVANT  
 UNE TRANSPLANTATION DE CELLULES SOUCHES ALLOGENIQUES  
 INVENTOR(S): SLAVIN, Shimon  
 PATENT ASSIGNEE(S): BAXTER INTERNATIONAL INC.;  
 HADASIT MEDICAL RESEARCH SERVICES AND DEVELOPMENT LTD.;  
 SLAVIN, Shimon  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9637208	A1	19961128

DESIGNATED STATES  
 W: AU CA JP MX NO US AT BE CH DE DK ES FI FR GB GR IE IT  
 LU MC NL PT SE  
 APPLICATION INFO.: WO 1996-US7652 A 19960524  
 PRIORITY INFO.: US 1995-8/449,764 19950525  
 ABEN Methods and materials are described for treating cancer patients with  
 solid tumors who have  
 undergone a cancer therapy regimen including allogeneic bone marrow  
 transplantation. Allogeneic  
 lymphocytes are administered to such patients. Patients with solid  
 tumors and patients with  
 hematopoietic tumors also may be treated with allogeneic lymphocytes  
 pre-activated by exposure in  
 vitro to a T-cell activator. The same or a different T-cell activator  
 additionally can be  
 administered to the patient in vivo.  
 ABFR L'invention se rapporte a des procedes et a des materiaux destines a  
 etre utilises dans le  
 traitement de patients atteints d'un cancer et presentant des tumeurs  
 solides, ces patients ayant  
 subi un traitement therapeutique, y compris une transplantation de  
 moelle osseuse allogenique. Des  
 lymphocytes allogeniques sont administres a ces patients. Des patients

presentant des tumeurs  
solides et des patients presentant des tumeurs hematopoietiques peuvent  
egalement etre traitees au  
moyen de lymphocytes allogeniques pre-actives par une exposition in  
vitro a un activateur de  
lymphocytes T. Le meme activateur de lymphocytes T ou un autre peut  
etre, de plus, administre au  
patient in vivo.

L33 ANSWER 41 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1996006165 PCTFULL ED 20020514  
TITLE (ENGLISH): GENETICALLY ENGINEERED SWINE CELLS  
TITLE (FRENCH): CELLULES PORCINES TRAITEES PAR GENIE GENETIQUE  
INVENTOR(S): SACHS, David, H.;  
SYKES, Megan;  
BAETSCHER, Manfred  
PATENT ASSIGNEE(S): THE GENERAL HOSPITAL CORPORATION;  
BIOTRANSPLANT, INC.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9606165	A1	19960229

DESIGNATED STATES

W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT  
SE

APPLICATION INFO.: WO 1995-US10250 A 19950810  
PRIORITY INFO.: US 1994-8/292,565 19940819

ABEN A genetically engineered cell for inducing tolerance.  
ABFR Cellules porcines traitees par genie genetique induisant la tolerance  
aux transplants.

L33 ANSWER 42 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1996005319 PCTFULL ED 20020514  
TITLE (ENGLISH): GENETICALLY ENGINEERED CELLS THAT PRODUCE DOPAMINE  
TITLE (FRENCH): CELLULES OBTENUES PAR GENIE GENETIQUE ET PRODUISANT DE  
LA DOPAMINE  
INVENTOR(S): KANG, Un, Jung;  
GAGE, Fred, H.  
PATENT ASSIGNEE(S): ARCH DEVELOPMENT CORPORATION;  
KANG, Un, Jung;  
GAGE, Fred, H.  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9605319	A1	19960222

DESIGNATED STATES

W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL  
PT SE

APPLICATION INFO.: WO 1995-US10291 A 19950811  
PRIORITY INFO.: US 1994-8/290,028 19940812

ABEN The present invention provides a process of increasing dopamine  
production in a cell comprising  
co-transfecting the cell with one or more expression vectors containing  
polynucleotides that encode  
tyrosine hydroxylase, aromatic L-amino acid decarboxylase and GTP  
cyclohydrolase. Cells transfected  
with such vectors and the use of such transformed cells to increase  
dopamine production in the  
central nervous system of animals are also provided.  
ABFR Procédé permettant de stimuler la production de dopamine dans une  
cellule. Ce procédé consiste  
à co-transfecter la cellule avec un ou plusieurs vecteurs d'expression  
renfermant des  
polynucleotides codant la tyrosine-hydroxylase, la L-aminoacide-  
decarboxylase aromatique et la  
guanosine triphosphate-cyclohydrolase. L'invention porte également sur  
des cellules transfectées à

l'aide de tels vecteurs et sur l'utilisation de telles cellules transformees pour accroitre la production de dopamine dans le systeme nerveux central.

L33 ANSWER 43 OF 63 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
DUPLICATE 5

ACCESSION NUMBER: 1996:377790 BIOSIS  
DOCUMENT NUMBER: PREV199699100146  
TITLE: A mathematical model for the estimation of human embryonic and fetal age.  
AUTHOR(S): Evtouchenko, L.; Studer, L.; Spenger, C. [Reprint author]; Dreher, E.; Seiler, R. W.  
CORPORATE SOURCE: Dep. Neurosurg., Univ. Bern, Inselspital, Freiburgstrasse, CH-3010 Bern, Switzerland  
SOURCE: Cell Transplantation, (1996) Vol. 5, No. 4, pp. 453-464. ISSN: 0963-6897.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 26 Aug 1996  
Last Updated on STN: 26 Aug 1996

AB Precise determination of donor age in human embryonic and fetal tissue is crucial for cell transplantation due to the existence of distinct time windows within which successful grafting is possible. This study demonstrates that between 4-12 wk postconception embryonic and fetal age can be estimated based on various morphometric parameters measured on a routine basis in suction abortion material. The greatest length, the neck-rump length, the foot length, and the proximal and distal arm and leg length were correlated with the anamnestic and ultrasonographically estimated age. Multivariate regression analyses showed a linear correlation between age and the logarithmic value of the various morphometric parameters. The best correlation was found for a mathematical model combining the limb parameters ( $r = 0.904$ ;  $p < 0.001$ ;  $n = 37$ ). A prospective follow-up study ( $n = 40$ ) was carried out to test the validity of the mathematical model. A high correlation was found between the calculated age and the estimated age based on anamnestic data ( $r = 0.749$ ,  $p < 0.001$ ). Outliers due to errors in the anamnestic data were readily identified by comparing anamnestic with calculated age. This method allows determination of embryonic and fetal age within and beyond the age group of the Carnegie classification and may, therefore, be useful for the needs of experimental and clinical cell transplantation.

L33 ANSWER 44 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
ACCESSION NUMBER: 1995012317 PCTFULL ED 20020514  
TITLE (ENGLISH): IMPROVED POSTANATAL AND IN UTERO FETAL HEMATOPOIETIC STEM CELL TRANSPLANTATION METHODS  
TITLE (FRENCH): PROCEDES DE TRANSPLANTATION IN UTERO ET POSTNATALE DE CELLULES SOUCHES HEMATOPIETIQUES FOETALE  
INVENTOR(S): HARRISON, Michael, R.;  
RICE, Henry, E.  
PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA  
LANGUAGE OF PUBL.: English  
DOCUMENT TYPE: Patent  
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9512317	A1	19950511

DESIGNATED STATES

W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE  
HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW NL NO  
NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN KE MW SD SZ  
AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ  
CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1994-US11557 A 19941012  
PRIORITY INFO.: US 1993-8/147,528 19931105

ABEN The application concerns improved postnatal and in utero fetal hematopoietic stem cell (HSC) transplantation methods. The application further concerns a method for the ex vivo expansion of fetal HSC using an artificial capillary system (ACS). Also, the application concerns a xenograft



system for confirming the presence of fetal HSC after expansion in an ACS cartridge. A method for transducing ex vivo expanding fetal HSC with packaged recombinant retrovirus vectors is also provided.

ABFR L'invention concerne des procedes de transplantation postnatale et in utero de cellules souches hematopoietiques foetales, ainsi qu'un procede d'expansion ex vivo de cellules souches hematopoietiques foetales a l'aide d'un systeme capillaire artificiel. L'invention porte egalement sur un systeme de xenogreffe permettant de confirmer la presence de cellules souches hematopoietiques foetales apres leur expansion dans une cartouche de systeme capillaire artificiel, et sur un procede de transduction ex vivo des cellules souches hematopoietiques foetales en expansion a l'aide de vecteurs de retrovirus recombines encapsides.

L33 ANSWER 45 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 6

ACCESSION NUMBER: 95371950 EMBASE

DOCUMENT NUMBER: 1995371950

TITLE: Development of the human striatum: Implications for fetal striatal transplantation in the treatment of Huntington's disease.

AUTHOR: Freeman T.B.; Sanberg P.R.; Isacson O.

CORPORATE SOURCE: Division of Neurosurgery, Pharmacol./Exptl. Therapeutics Dept., University of South Florida, 4 Columbia Drive, Tampa, FL 33606, United States

SOURCE: Cell Transplantation, (1995) 4/6 (539-545).

ISSN: 0963-6897 CODEN: CTRAE8

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 008 Neurology and Neurosurgery

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Fetal neural transplantation has recently been demonstrated to ameliorate motor and other behavioral deficits in animal models of Huntington's disease, and reconstruct many of the damaged striatal circuits. However, there has been significant variability in the histological appearance of these grafts, most likely related to differences of the regions of dissection of the donor tissue. Selective dissection and transplantation of the lateral ventricular eminence in rodents has resulted in grafts consisting of primarily striatal-like tissue. This data, combined with data from our own and other laboratories has led to a description of the development of the human striatum, with a particular emphasis on the relevance of human striatal development to the field of fetal tissue transplantation for the treatment of Huntington's disease. If the goal of transplantation is to graft GABAergic striatal projection neurons, it is our impression that optimal grafting results will occur when transplants are derived from the lateral ventricular eminence and the lateral aspect of the body of the ventricular eminence anterior to the foramen of Monro. Optimal results are likely to occur when donor ages range from Stage 19 to 23, with possible graft success when donor age extends to as late as postovulatory week 22.

L33 ANSWER 46 OF 63 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 95:371321 SCISEARCH

THE GENUINE ARTICLE: QY120

TITLE: GRAFTS AND THE ART OF MINDS RECONSTRUCTION - AUTHORS RESPONSE

AUTHOR: SINDEN J D (Reprint); HODGES H; GRAY J A

CORPORATE SOURCE: INST PSYCHIAT, DEPT PSYCHOL, DE CRESPIGNY PK, LONDON SE5 8AF, ENGLAND (Reprint)

COUNTRY OF AUTHOR: ENGLAND

SOURCE: BEHAVIORAL AND BRAIN SCIENCES, (MAR 1995) Vol. 18, No. 1, pp. 79-86.

ISSN: 0140-525X.  
DOCUMENT TYPE: Discussion; Journal  
FILE SEGMENT: SOCSEARCH; LIFE  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 62

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The use of neural transplantation to alleviate cognitive deficits is still in its infancy. We have an inadequate understanding of the deficits induced by different types of brain damage and their homologies in animal models against which to assess graft-induced recovery, and of the ways in which graft growth and function are influenced by factors within the host brain and the environment in which the host is operating. Further, use of fetal tissue may only be a transitory phase in the search for appropriate donor sources. Nevertheless, findings from our laboratory and elsewhere have made a prima facie case for successful cognitive reconstruction by graft methods.

L33 ANSWER 47 OF 63 USPATFULL on STN

ACCESSION NUMBER: 94:28683 USPATFULL  
TITLE: Genetically modified tyrosine hydroxylase and uses thereof  
INVENTOR(S): Goldstein, Menek, New York, NY, United States  
Wu, Jing, New York, NY, United States  
Filer, David, New York, NY, United States  
Friedhoff, Arnold J., New York, NY, United States  
PATENT ASSIGNEE(S): New York University, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5300436		19940405
APPLICATION INFO.:	US 1993-9075		19930126 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1991-669446, filed on 13 Mar 1991, now patented, Pat. No. US 5212082		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Wax, Robert A.		
ASSISTANT EXAMINER:	Hendricks, Keith D.		
LEGAL REPRESENTATIVE:	Browdy and Neimark		
NUMBER OF CLAIMS:	14		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 9 Drawing Page(s)		
LINE COUNT:	1275		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Modification of the DNA encoding the enzyme tyrosine hydroxylase (TH) resulting in amino acid substitution in one of the first fifty five N-terminal residues, in particular replacing Ser-40 with Tyr or Leu, produced TH variants having substantially increased enzymatic activity upon transfection of suitable host cells. Cells transfected with the variant TH having enhanced enzymatic activity are useful for treating neurological or psychiatric disorders associated with deficient TH or dopamine, in particular Parkinson's disease, by grafting such cells into the brain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L33 ANSWER 48 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 94237352 EMBASE  
DOCUMENT NUMBER: 1994237352  
TITLE: Fetal tissue research and prenatal fetal therapy: Ethical dilemmas.  
AUTHOR: Still L.  
CORPORATE SOURCE: Department of Diagnostic Ultrasound, Bellevue Community College, 3000 Landerholm Circle SE, Bellevue, WA 98007, United States  
SOURCE: Journal of Diagnostic Medical Sonography, (1994) 10/4 (208-212).  
ISSN: 8756-4793 CODEN: JDMSE2  
COUNTRY: United States

DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 049 Forensic Science Abstracts  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB **Fetal tissue** research was a volatile political issue during the Reagan and Bush administrations. The recent lifting of the federal moratorium banning such research raises many ethical questions. Recent advances in fetal therapy make it possible to cure fetal disease in utero. Ethical issues of **fetal tissue transplantation**, maternal-fetal rights, and resource allocation are discussed.

L33 ANSWER 49 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 7

ACCESSION NUMBER: 94105810 EMBASE  
DOCUMENT NUMBER: 1994105810  
TITLE: Suprachiasmatic nucleus lesions abolish and fetal grafts restore circadian gnawing rhythms in hamsters.  
AUTHOR: Le Sauter J.; Silver R.  
CORPORATE SOURCE: Barnard College, Columbia University, 3009 Broadway, New York, NY 10027, United States  
SOURCE: Restorative Neurology and Neuroscience, (1994) 6/2 (135-143).  
ISSN: 0922-6028 CODEN: RNNEEL

COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB It is widely accepted that the suprachiasmatic nuclei (SCN) of the hypothalamus serve as biological pacemakers, organizing daily activities. However some circadian rhythms are controlled by extra-SCN structures. **Transplantation** of fetal donor SCN in SCN-lesioned rodents induces recovery of rhythmic locomotor and drinking activities. **Such** grafts do not however, restore appropriate gonadal responses to photoperiodic stimuli. It is not known whether other behavioral rhythms are restored by fetal tissue grafts, or whether various responses are restored simultaneously. In the present study, we established that circadian rhythms of gnawing behavior are abolished following SCN lesions. Next, we measured both gnawing and wheel-running activity in SCN-lesioned hamsters following **transplantation** of fetal hypothalamic grafts containing the SCN. The results indicate that **such** grafts restore circadian rhythms of gnawing behavior, and that gnawing and wheel-running rhythms re-emerge at about the same time.

L33 ANSWER 50 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 8

ACCESSION NUMBER: 94133447 EMBASE  
DOCUMENT NUMBER: 1994133447  
TITLE: Attitudes of women to fetal tissue research.  
AUTHOR: Anderson F.; Glasier A.; Ross J.; Baird D.T.  
CORPORATE SOURCE: Family Planning and Women's Health, Lothian Health Board, Edinburgh, United Kingdom  
SOURCE: Journal of Medical Ethics, (1994) 20/1 (36-40).  
ISSN: 0306-6800 CODEN: JMETDR

COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 010 Obstetrics and Gynecology  
049 Forensic Science Abstracts  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB The use of human fetal tissue for scientific research has enormous potential but is subject to government legislation. In the United Kingdom the Polkinghorne Committee's guidelines were accepted by the Department of Health in 1990. These guidelines set out to protect women undergoing termination of pregnancy from exploitation but in so doing may significantly restrict potential research. Although the committee took evidence from a wide variety of experts they did not seek the views of the general public. We asked 108 women about to have a therapeutic abortion; 167 women who had had a pregnancy terminated in the past and 419 women who had never had an abortion their views on research

using human fetal tissue. Regardless of their past experiences the women were overwhelmingly in favour of research using fetal tissue (94 per cent). They made little distinction between basic research and research with obvious clinical relevance and supported the concept of using transplanted fetal tissue for the treatment of adult disease such as Parkinsonism. Women about to undergo an abortion were significantly more likely ( $p < 0.001$ ) to approve of all types of research including that aimed at improving methods of abortion and research using live fetuses in utero.

L33 ANSWER 51 OF 63 PCTFULL COPYRIGHT 2004 Univentio on STN  
 ACCESSION NUMBER: 1993014790 PCTFULL ED 20020513  
 TITLE (ENGLISH): A METHOD FOR TRANSPLANTING CELLS INTO THE BRAIN AND  
 THERAPEUTIC USES THEREFOR  
 TITLE (FRENCH): PROCEDE DE TRANSPLANTATION DE CELLULES DANS LE CERVEAU  
 ET UTILISATIONS THERAPEUTIQUES DE CE PROCEDE  
 INVENTOR(S): CHERKSEY, Bruce, D.  
 PATENT ASSIGNEE(S): NEW YORK UNIVERSITY  
 LANGUAGE OF PUBL.: English  
 DOCUMENT TYPE: Patent  
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9314790	A1	19930805

# DESIGNATED STATES

W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT  
 SE

APPLICATION INFO.: WO 1993-US494 A 19930121  
 PRIORITY INFO.: US 1992-823,654 19920123

ABEN A method for grafting a cell in the brain of a mammalian subject is accomplished by attaching the cell to a support matrix so that the cell attaches to the matrix surface, and implanting the support matrix with the attached cell into the brain. Preferred support matrices are glass or plastic microbeads, either solid or porous, having a diameter from about 90 to about 125  $\mu\text{m}$ . The method employs cells of different types, preferably cells of neural or paraneural origin, such as adrenal chromaffin cells. Also useful are cell lines grown in vitro. Cells not of neural or paraneural origin, such as fibroblasts, may also be used following genetic alteration to express a desired neural product such as a neurotransmitter or a neuronal growth factor. The method is used to treat neurological diseases such as Parkinson's disease, Alzheimer's disease, Huntington's disease, epilepsy, and traumatic brain injury.

ABFR Selon un procede destine a greffer une cellule dans le cerveau d'un mammifere, on fixe la cellule a une matrice support de facon a ce que la cellule se fixe a la surface de la matrice, et on implante dans le cerveau la matrice support et la cellule fixee. Les matrices support preferees sont en verre ou sont faites de microbilles en plastique, solides ou poreuses, d'un diametre d'environ 90 a environ 125  $\mu\text{m}$ . Ce procede utilise des cellules de types differents, de preference des cellules d'origine neurale ou paraneurale, telles que des cellules chromaffines surrenales. On utilise egalement des lignees cellulaires cultivees in vitro. Les cellules qui ne sont pas d'origine neurale ou paraneurale, telles que des fibroblastes, peuvent etre egalement utilisees selon la modification genetique pour exprimer un produit neural desire tel qu'un neurotransmetteur ou un facteur de croissance neuronal. Le procede est utilise pour traiter des maladies neurologiques telles que la maladie de Parkinson, la maladie d'Alzheimer, la maladie d'Huntington, l'epilepsie et les lesions

traumatiques du cerveau.

L33 ANSWER 52 OF 63 USPATFULL on STN

ACCESSION NUMBER: 93:39908 USPATFULL

TITLE: Genetically modified tyrosine hydroxylase and uses thereof

INVENTOR(S): Goldstein, Menek, New York, NY, United States

Wu, Jing, New York, NY, United States

Filer, David, New York, NY, United States

Friedhoff, Arnold J., New York, NY, United States

PATENT ASSIGNEE(S): New York University, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5212082		19930518
APPLICATION INFO.:	US 1991-669446		19910313 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Wax, Robert A.		
ASSISTANT EXAMINER:	Hendricks, Keith D.		
LEGAL REPRESENTATIVE:	Browdy and Neimark		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 9 Drawing Page(s)		
LINE COUNT:	1070		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Modification of the DNA encoding the enzyme tyrosine hydroxylase (TH) resulting in amino acid substitution in one of the first fifty five N-terminal residues, in particular replacing Ser-40 with Tyr or Leu, produced TH variants having substantially increased enzymatic activity upon transfection of suitable host cells. Cells transfected with the variant TH having enhanced enzymatic activity are useful for treating neurological or psychiatric disorders associated with deficient TH or dopamine, in particular Parkinson's disease, by grafting such cells into the brain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L33 ANSWER 53 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 9

ACCESSION NUMBER: 91146914 EMBASE

DOCUMENT NUMBER: 1991146914

TITLE: Cellular replacement therapy for neurologic disorders: Potential of genetically engineered cells.

AUTHOR: Chen L.S.; Ray J.; Fisher L.J.; Kawaja M.D.; Schinstine M.; Kang U.J.; Gage F.H.

CORPORATE SOURCE: Dept. of Neurosciences, University of California, San Diego, La Jolla, CA 92093, United States

SOURCE: Journal of Cellular Biochemistry, (1991) 45/3 (252-257).  
ISSN: 0730-2312 CODEN: JCEBD5

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 008 Neurology and Neurosurgery

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Neural transplantation, a mode of cellular replacement, has been used as a therapeutic trial for Parkinson's disease. Studies indicate that tonic release of the metabolites from the graft that can be utilized by the host brain, is likely to be the major mechanism responsible for the therapeutic effect. The use of fetal tissue is complicated by ethical controversy and immunological incompatibility. Autografting adult tissue has not been successful mainly due to poor survival. Genetically engineered cells are promising alternative sources of donor cells. We have investigated the potential of primary skin fibroblasts as donor cells for intracerebral grafting. Primary skin fibroblasts survive in the brain and remain in situ. A number of genes (nerve growth factor, tyrosine hydroxylase, glutamic acid decarboxylase, and choline acetyltransferase) have been successfully introduced and expressed in the primary fibroblasts. The L-dopa-secreting primary fibroblasts exhibited a behavioral effect in

a rat model of Parkinson's disease up to 8 weeks after being grafted into denervated striatum. Factors that can maximize gene transfer, transgene expression, and fibroblast survival in the brain make up to the future direction of investigation.

L33 ANSWER 54 OF 63 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 91174741 EMBASE  
DOCUMENT NUMBER: 1991174741  
TITLE: Effects of cool storage on survival and function of  
intrastratial ventral mesencephalic grafts.  
AUTHOR: Sauer H.; Brundin P.  
CORPORATE SOURCE: Department of Medical, Physiology, University of Munich,  
Pettenkoferstr. 12, D-8000 Munich 2, Germany  
SOURCE: Restorative Neurology and Neuroscience, (1991) 2/3  
(123-135).  
ISSN: 0922-6028 CODEN: RNNEEL  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
021 Developmental Biology and Teratology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Ongoing clinical trials with **fetal tissue transplants** in Parkinson's disease would be facilitated by an effective tissue storage technique that would allow for temporal separation of the procurement of the fetal **donor** tissue and implantation surgery. In order to develop **such** a method, we grafted rat or human fetal ventral mesencephalic tissue to the dopamine-depleted striatum of rats either directly, or following pregraft refrigeration in a 'hibernation' medium at 4°C. Rat tissue **transplants** were found to normalize amphetamine-induced circling behavior at 6 weeks post-transplantation after having been hibernated for either 2 or 5 days. The number of tyrosine hydroxylase immunoreactive neurons in these hibernated grafts did not differ significantly from that found in matched grafts of fresh tissue. Hibernation for 10 days resulted both in an absence of functional effects and in decreases of graft survival down to 10-20% of control values. Volume assessment of fresh and hibernated grafts prepared from human **fetal tissue** revealed no adverse effects of a 3 day hibernation interval at 3 weeks after **transplantation** into immunosuppressed rats. The results indicate that hibernation of neural tissue may be a convenient and simple tool, which can help to guarantee tissue availability at the planned time of implantation in patients and facilitate transport and bacteriological examination. Furthermore, the method offers a simple means which permits prolonged exposure of the neural tissue to trophic factors and specific markers prior to grafting in experimental animals.

L33 ANSWER 55 OF 63 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 91:353312 SCISEARCH  
THE GENUINE ARTICLE: FR396  
TITLE: EFFECTS OF COOL STORAGE ON SURVIVAL AND FUNCTION OF  
INTRA-STRIAL VENTRAL MESENCEPHALIC GRAFTS  
AUTHOR: SAUER H (Reprint); BRUNDIN P  
CORPORATE SOURCE: UNIV MUNICH, DEPT MED PHYSIOL, PETTENKOFERSTR 12, W-8000  
MUNICH 2, GERMANY (Reprint); UNIV LUND, DEPT MED CELL RES,  
S-22101 LUND, SWEDEN  
COUNTRY OF AUTHOR: GERMANY; SWEDEN  
SOURCE: RESTORATIVE NEUROLOGY AND NEUROSCIENCE, (1991) Vol. 2, No.  
3, pp. 123-135.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 49

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Ongoing clinical trials with **fetal tissue transplants** in Parkinson's disease would be facilitated by an effective tissue storage technique that would allow for temporal separation of the procurement of the fetal **donor** tissue and implantation surgery. In order to develop **such** a method, we

grafted rat or human fetal ventral mesencephalic tissue to the dopamine-depleted striatum of rats either directly, or following pregraft refrigeration in a 'hibernation' medium at 4-degrees-C. Rat tissue **transplants** were found to normalize amphetamine-induced circling behavior at 6 weeks post-**transplantation** after having been hibernated for either 2 or 5 days. The number of tyrosine hydroxylase immunoreactive neurons in these hibernated grafts did not differ significantly from that found in matched grafts of fresh tissue. Hibernation for 10 days resulted both in an absence of functional effects and in decreases of graft survival down to 10-20% of control values. Volume assessment of fresh and hibernated grafts prepared from human **fetal tissue** revealed no adverse effects of a 3 day hibernation interval at 3 weeks after **transplantation** into immunosuppressed rats. The results indicate that hibernation of neural tissue may be a convenient and simple tool, which can help to guarantee tissue availability at the planned time of implantation in patients and facilitate transport and bacteriological examination. Furthermore, the method offers a simple means which permits prolonged exposure of the neural tissue to trophic factors and specific markers prior to grafting in experimental animals.

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on STN

ACCESSION NUMBER: 90261091 EMBASE

DOCUMENT NUMBER: 1990261091

TITLE: Comparison of growth, neovascularization, and enzymatic function of fetal intestinal grafts in the omentum and renal capsule.

AUTHOR: Tisinai K.; Shedd F.; Harris R.; Unthank J.; Grosfeld J.; Abu-Dalu K.; Grosfeld J.L.

CORPORATE SOURCE: Section of Pediatric Surgery, Indiana University Medical Center, Indianapolis, IN, United States

SOURCE: Journal of Pediatric Surgery, (1990) 25/8 (914-916).

ISSN: 0022-3468 CODEN: JPDSA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

**AB Fetal tissues** are less immunogenic and may be a useful **donor** source for organ **transplantation**. This report compares the fate of fetal small bowel segments **transplanted** in the omentum and renal capsule of recipient syngeneic rats. Two-centimeter segments of fetal jejunum and ileum were obtained from 26 **donor** 19-day gestational age rat fetuses and **transplanted** into the subrenal capsule (n = 35) and omentum (n = 40) in syngeneic Fisher rats (weight, 150 g) as free grafts. No immunosuppression was used. At 2 weeks posttransplantation, the recipient rats underwent laparotomy and the grafts were evaluated for viability, growth, enzymatic function, and revascularization. Viable grafts were identified in 27 of 35 renal capsule grafts and 34 of 40 omental grafts. The order of magnitude of fetal growth in the omentum for jejunum was  $16 \pm 10$  versus ileum  $23 \pm 9$  (NS). However, in the renal capsule, ileal growth ( $15 \pm 6$ ) was significantly greater than jejunum ( $8 \pm 5$ ;  $P < .01$ ). Growth for both jejunal and ileal segments was greater in the omentum ( $P < .02$ ). The lumen of all omental grafts remained patent; however, 26 of 27 renal grafts had cystic dilatations and areas of obstruction. Microfil casts of the specimens showed vascular connections (neovascularization) between the graft and omentum, a normal serosal vascular pattern, and many submucosal capillary-like vessels. Maltase activity was measured in fetal grafts and compared with control pups bred on the same date as the **donor** animals. The grafts had a higher maltase level  $33.4 \pm 34.6$   $\mu\text{mol}/\text{min}/\text{g}$  than controls  $8.3 \pm 2.0$  ( $P < .005$ ). Maltase activity between control jejunum and ileum was similar ( $7.7 \pm 1.5$  v  $9.0 \pm 2.3$  [NS]). Fetal jejunal specimens ( $51.2 \pm 41.9$ ) had greater maltase activity than ileum ( $15.6 \pm 6.7$ ;  $P < .005$ ). Maltase in fetal ileum was similar in omentum and renal capsule; however, jejunal maltase was significantly higher in the renal site ( $85.0 \pm 45.7$ ) versus omentum ( $25.0 \pm 10.0$ ;  $P < .02$ ). These data indicate that fetal intestinal grafts can be successfully (78% to 86%) implanted in an intraabdominal site in syngeneic recipients. Growth of fetal grafts,

neovascularity, and enzymatic function (jejunum > ileum) were documented in both the renal capsule and omentum; however, bowel morphology and luminal patency was better in the omentum. These observations suggest that free-fetal bowel grafts may have a potential role in bowel transplantation.

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on STN

ACCESSION NUMBER: 88157898 EMBASE  
DOCUMENT NUMBER: 1988157898  
TITLE: Bone marrow transplantation in the treatment of severe immunodeficiencies: Possibilities and problems.  
AUTHOR: Vossen J.M.  
CORPORATE SOURCE: Department of Pediatrics, University Hospital Leiden, Leiden, Netherlands  
SOURCE: Immunological Investigations, (1988) 17/2 (135-146).  
ISSN: 0882-0139 CODEN: IMINEJ  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Infants and children suffering from severe primary immunodeficiencies may be cured by bone marrow transplantation from a healthy donor. Data obtained in 14 European centers show that about 60% of the patients are surviving disease-free, if they were grafted with bone marrow cells from an HLA-identical related donor. Results of transplantation of T-cell depleted bone marrow from an HLA-haploidentical related donor were also excellent in infants with severe combined immunodeficiency, with 60% recovery. This therapy is superior to transplantation of fetal tissues. HLA-haploidentical T-cell depleted marrow transplantation for other severe immunodeficiencies was less successful. This was mainly due to failure of engraftment, despite intensive conditioning of the recipient, and to infectious complications e.g. by reactivation of latently present viruses.

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ACCESSION NUMBER: 85219198 EMBASE  
DOCUMENT NUMBER: 1985219198  
TITLE: Transplantation of organ-cultured fetal pancreas: Experimental studies and potential clinical application in diabetes mellitus.  
AUTHOR: Mandel T.E.  
CORPORATE SOURCE: Transplantation Unit, Walter and Eliza Hall Institute of Medical Research, Royal Melbourne Hospital, Vic. 3050, Australia  
SOURCE: World Journal of Surgery, (1984) 8/2 (158-168).  
CODEN: WJSUDI  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 009 Surgery  
006 Internal Medicine  
003 Endocrinology  
LANGUAGE: English

AB Transplantation of organ-cultured fetal islets of Langerhans may be one way of overcoming the dual difficulties of finding a suitable source of tissue and controlling graft rejection. Experiments in mice have clearly shown that fetal pancreas is an excellent source of islets. Tissue from one donor can be used to treat one or more recipients and provides excellent control of drug-induced diabetes, including prevention of diabetic renal microangiopathy. The fetal islets display selective survival in vitro and organ culture can be used to obtain large amounts of tissue for transplantation. In addition, growth in 'normoglycemic' media results in functional maturation of the fetal tissue. Culture conditions can be modified to eliminate from the putative graft immunogenic 'passenger leukocytes', the cells responsible for initiating graft rejection. Such immunogenic cell-depleted grafts can be transplanted across histocompatibility barriers without the need for recipient



immunosuppression. Fetal human pancreas shares many properties in common with fetal mouse pancreas. Continuing growth and differentiation occur in vitro and following xenotransplantation into athymic mice. However, fetal human pancreas is frequently damaged by ischemia before it can be used, and also appears to be more susceptible to oxygen toxicity than is fetal mouse pancreas. Nevertheless, when fresh human tissue is available, it may be a suitable source of islets for **transplantation** in type I diabetics.

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ACCESSION NUMBER: 83144014 EMBASE  
DOCUMENT NUMBER: 1983144014  
TITLE: Growth, differentiation, and viability of fetal rat cortical and spinal cord implants into adult rat spinal cord.  
AUTHOR: Patel U.; Bernstein J.J.  
CORPORATE SOURCE: VA Med. Cent., Washington, DC 20422, United States  
SOURCE: Journal of Neuroscience Research, (1983) 9/3 (303-310).  
CODEN: JNREDK  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology  
002 Physiology  
021 Developmental Biology and Teratology  
008 Neurology and Neurosurgery  
LANGUAGE: English

AB **Successful** transplantation of the fetal brain into adult host brain has been accomplished. These studies explore the growth, differentiation, and viability of E11, E12, and E15 rat fetal cortex and fetal spinal cord implantation into the spinal cord of adult rats (**donor** and host, Sprague Dawley). Under deep Chloropent anesthesia, 70 rats had 1-mm cubes of fetal cortex inserted with pressure or by stylus injection subpially between the dorsal horn and dorsal column (left side), or implantation of whole segments of fetal spinal cord. Animals were prepared for light microscopy 14 and 21 days and 1, 2, and 3 months later. Implants by both fetal tissues had a 69% survival rate. The younger the fetal implant the higher the **success** of the implant (E11>E15). The diameter of fetal spinal cord implants reached the diameter of control postnatal animals after 30 days. The implants not only increased in mass (up to 7-fold in some cases) but differentiated and matured (apolar, unipolar, bipolar and multipolar) neurons were observed one to three months postimplantation. By 30 days postimplantation, fetal neurons had large, often crenated nuclei, with a large single prominent nucleolus. The most **successful** implants were the young E11 fetal spinal cord into the adult host spinal cord. These implants represent an initial **successful** transplantation of fetal spinal cord into adult spinal cord.

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ACCESSION NUMBER: 82020229 EMBASE  
DOCUMENT NUMBER: 1982020229  
TITLE: Sex-associated differences in the immune response against fetal major histocompatibility antigens.  
AUTHOR: Tartakovsky B.; De Baetselier P.; Feldman M.; Segal S.  
CORPORATE SOURCE: Dept. Cell Biol., Weizmann Inst. Sci., Rehovot 76100, Israel  
SOURCE: Transplantation, (1981) 32/5 (395-397).  
CODEN: TRPLAU  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
LANGUAGE: English

AB Alloantibodies against H-2(b) and H-2(k) haplotypes were produced in C57BL/6J and C3H female and male mice in response to **transplantation** of F1 fetal tissue (bone) or adult F1 cells (spleen). Testing IgG1 and IgG2 antibodies by means of the fluorescence-activated cell sorter (FACS II), we found no differences between males and females in the isotype content of antisera produced against spleen cells from adult **donors**. In contrast, striking

sex-associated differences were found in the isotypes produced against fetal allografts: females produced much more IgG1 than males, although they produced comparable amounts of IgG2. Hence, it appears that females differ from males in their humoral alloreactivity against major histocompatibility complex (MHC) gene products expressed on fetal cells. **Such** MHC antigens expressed on fetal **tissues** seem to generate different immune signals than the MHC antigens expressed on adult cells. These observations might be of relevance to the biological role played by the IgG1 alloantibodies produced during pregnancy against the MHC alloantigens of the fetus.

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ACCESSION NUMBER: 80073193 EMBASE  
DOCUMENT NUMBER: 1980073193  
TITLE: Immunologic problems in islet transplantation.  
AUTHOR: Barker C.F.; Naji A.; Silvers W.K.  
CORPORATE SOURCE: Harrison Dept. Surg. Res., Sch. Med., Univ. Pennsylvania, Philadelphia, Pa., United States  
SOURCE: Diabetes, (1980) 29/SUPPL. 1 (86-92).  
CODEN: DIAEAZ  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 003 Endocrinology  
006 Internal Medicine  
026 Immunology, Serology and Transplantation  
009 Surgery  
048 Gastroenterology  
LANGUAGE: English

AB Rapid rejection of islet allografts is due to both cellular and antibody mechanisms. Isolated islets **transplanted** intraportally across a major histocompatibility complex (MHC) barrier in rats are rejected in 3-5 days. However, with MHC identity, the median survival time can be as long as 30.5 days. In mice isolated islets **transplanted** between H-2-compatible strains survive no more than 1 wk, only a few days more than with an H-2-incompatible cross. In addition, in certain strains of rats and mice, islet isografts from male **donors** are rejected by female recipients. Fetal pancreases **transplanted** beneath the kidney capsule (Lewis to Fisher) are rapidly rejected by 4 days, although longestablished grafts of fetal pancreas are not vulnerable to rejection in contrast to adult islets. Minimizing histoincompatibility has been unsuccessful in overcoming rejection because of the universal vulnerability of **transplanted** islets, and attempts to minimize immunogenicity by use of fetal tissue have not prevented rejection; however, culture of **donor** tissue may prove helpful in reducing immunogenicity. **Transplantation** of islet tissue into immunologically privileged sites has not resulted in reliable reversal of diabetes. Immunosuppression by pharmacologic agents **such** as cyclophosphamide, azathioprine, and corticosteroids was of minor effectiveness, but antilymphocytic serum was quite effective in rodents, even on xenografts when the injections were continued. Immunologic tolerance produced at birth by **donor** lymphopoietic cells permits later engraftment of isolated **donor** islets or whole pancreas. However, enhancement by antidonor antibody has not been greatly effective in protecting islets against rejection. The possibility that autoimmunity to islet tissue might interfere with the function of **transplanted** islets was tested in three types of possible autoimmunity: (1) repeated small doses of streptozotocin, (2) encephalomyocarditis virus, and (3) 'BB' rats. In all three cases, **transplanted** islets were effective in reversing experimental diabetes.

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ACCESSION NUMBER: 80133859 EMBASE  
DOCUMENT NUMBER: 1980133859  
TITLE: Bone marrow transplantation in Europe.  
AUTHOR: Touraine J.L.; Triau R.; Zwaan F.E.  
CORPORATE SOURCE: Claude Bernard Univ., Lyon, France  
SOURCE: (1979) (I-IX+224p.).  
COUNTRY: Netherlands

DOCUMENT TYPE: Book  
FILE SEGMENT: 025 Hematology  
LANGUAGE: English

AB In this book the papers presented at the second European symposium on bone marrow transplantation are reported. Methods for marrow transplantation in immunodeficiencies, aplastic anaemias, acute actute leukaemias and osteopetrosis are somewhat different as far as the conditioning regimen, the subsequent treatment and laboratory monitoring are concerned. Most immunobiological aspects (histocompatibility, prevention and treatment of graft versus host disease), isolation measures, and anti infection therapies are described. The overall European experience shows the best results in the severe combined immunodeficiency diseases. In the absence of a compatible donor, fetal tissue transplantation has resulted in immunological reconstitution of several patients. In aplastic anaemia, marrow transplantation has proved successful in 36% of the cases and encouraging results have been obtained with antilymphocyte globulin treatment. In acute leukaemia, allogeneic marrow transplantation has not yet provided comparable results. Infusion of autologous marrow, possibly treated in vivo, may prove to be an alternative.

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ACCESSION NUMBER: 78401501 EMBASE  
DOCUMENT NUMBER: 1978401501  
TITLE: Immunobiology of bone marrow transplantation.  
AUTHOR: Dicke K.A.; Lotzova E.; Spitzer G.; McCredie K.B.  
CORPORATE SOURCE: Dept. Developm. Therapeut., Univ. Texas Syst. Cancer Cent.,  
MD Anderson Hosp. Tum. Inst., Houston, Tex. 77030, United States  
SOURCE: Seminars in Hematology, (1978) 15/3 (263-282).  
CODEN: SEHEA3  
COUNTRY: United States  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 025 Hematology  
026 Immunology, Serology and Transplantation  
016 Cancer  
005 General Pathology and Pathological Anatomy  
LANGUAGE: English

AB Bone marrow transplantation is a special form of tissue transplantation in which four types of graft can be distinguished according to the immunogenetic relation between the host and the donor: 1.) autologous bone marrow grafts, 2.) isogeneic transplantation, 3.) allogeneic transplantation, and 4.) xenogeneic transplantation. In aplastic anemia, bone marrow transplants from identical twin donors are being used and are preferable to transplants from allogeneic donors; however, the frequency of availability of the identical twin donor is low, so that this type of transplantation is rare in comparison to the use of allogeneic bone marrow in this disease. The situation is the same for acute leukemia; however, in this disease there has been a renewed interest in the use of autologous bone marrow transplantation triggered by new developments in storage and separation techniques of bone marrow cells collected during remission. In the majority of cases of solid tumors, in the absence of tumor invasion of the bone marrow, autologous marrow cells are available. These cells can be collected and stored effectively before the administration of high-dose chemotherapy. The subsequent reinfusion of the thawed bone marrow cells can then be used to prevent prolonged suppression of the hemopoietic system. Serious complications immediately after allogeneic bone marrow transplantation are related to the acute GVH reaction. Methods to mitigate and prevent GVH reactions fall into two major categories: selection of the donor on the basis of histocompatibility testing and described: in this context only the most effective and commonly used methods will be mentioned. They are (1) donor selection, (2) treatment of the recipient by weekly intravenous administration of methotrexate, (3) elimination of lymphocytes from the bone marrow cell suspension before transplantation, (4) bacteriologic decontamination of the recipient, and (5) the use of fetal liver as a source for HSC. The acute GVH problem has been substantially

diminished by the development of a cell fractionation technique (discontinuous albumin gradient centrifugation). This technique, takes advantage of differences in cellular density between stem cells and lymphocytes. In the patient population with leukemia treated with fractionated marrow, lifespan was still short owing to complications other than GVH. The patients in this group consisted of endstage patients with severely compromised immunologic and hematologic functions making them extremely prone to bacterial and viral infections both before and during the immediate posttransplantation period. According to the bone marrow registry, 69 SCID patients have been grafted with hemopoietic cells. **Transplantation** of marrow from HLA genetically identical **donors** provided the highest 6-mo survival rate (63%). Six-month survival rates for patients who received **fetal tissue transplants** (43%) or marrow from mixed leukocyte culture (MLC)-negative donors (38%) were significantly higher than for patients treated with marrow from MLC-positive **donors** (5%). The **transplantation** results in aplastic anemia are promising using bone marrow from MDC-identical siblings. In one series long-term survival is reported in 38% of the patients. Similar results are reported by other groups in the bone marrow **transplantation** registry. In solid tumors in man such as lymphoma and ovarian cancer the hemopoietic toxicity of high-dose chemotherapy had been significantly reduced by bone marrow **transplantation**. The extreme favorable results in terms of tumor cell control, absence of serious infections, and long-term tumor control without chemotherapy support the use of autologous bone marrow **transplantation** as a supportive measure to prevent lethal hemopoietic toxicity. (Newman - Bridgeport, Conn.)

=> d his

(FILE 'HOME' ENTERED AT 15:34:54 ON 20 JUL 2004)

FILE 'MEDLINE' ENTERED AT 15:35:04 ON 20 JUL 2004

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L1      6659 S FETAL TISSUE
L2      146532 S IN UTERO OR DONOR
L3      59250 S PERCUTAN?
L4      2 S L1 (S) L2 (S) 3
L5      0 S L1 (S) L2 (S) L3
L6      60 S L1 (S) L2
L7      23472 S INCISION
L8      0 S L1 (S) L2 (S) L7
L9      354581 S TRANSPLANT?
L10     14 S L1 (S) L2 (S) L9
L11     1197155 S SUCTION OR VACUUM OR SUC?
L12     1 S L1 (S) L2 (S) L9 (S) L11
L13     1406689 S SUCTION OR VACUUM OR SUC? OR REMOV?
L14     1 S L1 (S) L2 (S) L9 (S) L13
L15     247721 S ?CUTAN?
L16     0 S L1 (S) L2 (S) L9 (S) L15
L17     0 S L1 (L) L2 (L) L9 (L) L15
L18     21 S L1 (L) L2 (L) L9 (L) L13
L19     64 S L1 (L) L15
L20     64 S L1 (L) L15 (L) L19
L21     13 S L1 (L) L15 (L) L19 (L) L13
L22     59250 S PERCUTAN?
L23     0 S L1 (S) L22
L24     2 S L1 (L) L22
L25     79 S L2 (S) L22
L26     215420 S FETAL
L27     8 S L2 (S) L22 (S) L26

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FILE 'BIOSIS, EMBASE, CAPLUS, PCTFULL, USPATFULL, SCISEARCH, MEDLINE, CONFSCI' ENTERED AT 15:57:23 ON 20 JUL 2004

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L28     80 S L14
L29     69 DUP REM L28 (11 DUPLICATES REMOVED)
L30     5 S L16
L31     3 S L5
L32     74 S L12
L33     63 DUP REM L32 (11 DUPLICATES REMOVED)

```

=> logoff hold  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
206.91	235.21

FULL ESTIMATED COST

SESSION WILL BE HELD FOR 60 MINUTES  
STN INTERNATIONAL SESSION SUSPENDED AT 16:10:36 ON 20 JUL 2004